

WASHINGTON STATE HEALTH CARE AUTHORITY

# Spinal Injections

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## Health Technology Assessment

**UPDATED FINAL EVIDENCE REPORT**  
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# Spinal Injections

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This technology assessment report is based on research conducted by a contracted technology assessment center, with updates as contracted by the Washington State Health Care Authority. This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the investigators and authors who are responsible for the content. These findings and conclusions may not necessarily represent the views of the HCA/Agency and thus, no statement in this report shall be construed as an official position or policy of the HCA/Agency.

The information in this assessment is intended to assist health care decision makers, clinicians, patients and policy makers in making sound evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

## TABLE OF CONTENTS

<b>EXECUTIVE SUMMARY .....</b>	<b>10</b>
<b>1. Appraisal .....</b>	<b>17</b>
1.1. Rationale .....	17
1.2. Key Questions.....	18
1.3. Outcomes Assessed.....	19
<b>2. Background .....</b>	<b>21</b>
2.1. The condition .....	21
2.2. The technology and its comparators.....	22
2.3. Mechanism of action.....	23
2.4. Injection procedures .....	23
2.5. Indications.....	25
2.6. Contraindications .....	26
2.7. Potential Complications and Harms .....	26
2.8. Clinical Guidelines.....	27
2.9. Previous Systematic Reviews/Technology Assessments .....	31
2.10. Medicare and Representative Private Insurer Coverage Policies.....	46
<b>3. The Evidence .....</b>	<b>56</b>
3.1. Methods of the Systematic Literature Review.....	56
3.2. Quality of Literature available .....	61
<b>4. Results .....</b>	<b>71</b>
<b>4.1. Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?.....</b>	<b>71</b>
Lumbar spinal injections.....	71
4.1.1. Lumbar interlaminar or caudal epidural injections versus placebo (saline/water and/or local anesthetic) controls.....	71
4.1.2. Lumbar transforaminal epidural injections versus placebo controls.....	81
4.1.3. Lumbar epidural steroid injections versus non-placebo controls.....	84
4.1.4. Lumbar facet interventions versus placebo (saline and/or local anesthetic) controls .....	91
4.1.5. Lumbar facet interventions versus non-placebo controls.....	92
4.1.6. Sacroiliac joint injections versus placebo (saline and/or local anesthetic) controls.....	95
4.1.7. Lumbar intradiscal injections versus placebo (saline and/or local anesthetic) controls .....	96
4.1.8. Lumbar intradiscal injections versus non-placebo controls .....	98
Cervical spinal injections.....	99
4.1.9. Cervical epidural injections versus placebo (saline and/or local anesthetic) controls.....	99

4.1.10	Cervical epidural injections versus non-placebo controls .....	103
4.1.11	Cervical facet interventions versus placebo (saline and/or local anesthetic) controls .....	105
4.1.12	Other potential comparisons.....	106
<b>4.2.</b>	<b>Key Question 2: What is the evidence of the safety of spinal injections? .....</b>	<b>107</b>
4.2.1.	Complications following lumbar spine injections .....	107
4.2.2.	Complications following cervical spine injections .....	108
4.2.3.	Complications following lumbar OR cervical spine injections .....	109
4.2.4.	Incidence of vascular puncture .....	109
4.2.5.	Radiation exposure to the physician.....	110
4.2.6.	Case reports of major adverse events following spinal injections .....	110
<b>4.3.</b>	<b>Key Question 3: What is the evidence that spinal injections have differential efficacy or safety issues in subpopulations?.....</b>	<b>112</b>
4.3.1.	Different approaches for administering lumbar epidural steroids in patients.....	112
4.3.2.	Diagnosis.....	114
4.3.3.	Baseline pain and dysfunction.....	115
4.3.4.	Injectate.....	115
4.3.5.	Other.....	116
<b>4.4.</b>	<b>Key Question 4: What is the evidence of cost implications and cost- effectiveness of spinal injections? .....</b>	<b>117</b>
4.4.1.	Background and context .....	117
4.4.2.	Description of included studies.....	133
<b>5.</b>	<b>Summary and Implications.....</b>	<b>136</b>
<b>REFERENCES</b> .....		<b>147</b>

## TABLES

Table 1. Outcome measures .....	19
Table 2: Overview of previous systematic reviews of spinal injections.....	32
Table 3. Overview of payer technology assessments and policies for spinal injections .....	51
Table 4. Summary of inclusion and exclusion criteria .....	58
Table 5. Pain and function outcomes from placebo-controlled trials of lumbar caudal or interlaminar epidural steroid injections for low back pain with sciatica or radiculopathy .....	74
Table 6. Pain and function outcomes from placebo-controlled trials of caudal or interlaminar epidural steroid injections for low back pain without radiculopathy.....	77
Table 7. Pain and function outcomes from placebo-controlled trials of caudal or interlaminar epidural steroid injections for spinal stenosis .....	79
Table 8. Pain and function outcomes from placebo-controlled trials of caudal or interlaminar epidural steroid injections for failed back surgery syndrome.....	80
Table 9. Pain and function outcomes from placebo-controlled trials of transforaminal epidural steroid injections for low back pain with radiculopathy .....	83
Table 10. Pain and function outcomes from trials comparing lumbar epidural steroid injections to non-placebo controls.....	88
Table 11. Pain and function outcomes from placebo-controlled trials of lumbar intraarticular facet joint injections.....	91
Table 12. Pain and function outcomes from placebo-controlled trials of lumbar therapeutic medial branch blocks .....	92
Table 13. Pain and function outcomes from trials of lumbar intraarticular facet joint injections or medial branch blocks versus non-placebo controls .....	93
Table 14. Pain and function outcomes from trials of sacroiliac joint injections versus placebo controls.....	95
Table 15. Pain and function outcomes from trials of lumbar intradiscal injections versus placebo controls.....	96
Table 16. Pain and function outcomes from trials of lumbar intradiscal injections versus non-placebo controls .....	98

Table 17. Pain and function outcomes from trials of cervical epidural steroid injections versus placebo controls for neck pain with disc herniation and radiculitis.....	99
Table 18. Pain and function outcomes from trials of cervical epidural steroid injections versus placebo controls for neck pain without disc herniation or radiculitis .....	102
Table 19. Pain and function outcomes from trials of cervical epidural steroid injections versus non-placebo controls for neck pain with disc herniation and radiculitis .....	103
Table 20. Pain and function outcomes from placebo-controlled trials of cervical intraarticular facet joint injections.....	105
Table 21. Pain and function outcomes from placebo-controlled trials of cervical therapeutic medial branch blocks .....	106
Table 22. Pain and satisfaction outcomes from one RCT <sup>93</sup> comparing epidural steroid injection administered by interlaminar (IL) versus transforaminal (TF) approaches stratified by diagnosis of herniated intervertebral disc (HIVD) or spinal stenosis (SS).....	113
Table 23. Summary of evidence for Key Question 1.....	136
Table 24. Summary of evidence for Key Question 2.....	142
Table 25. Summary of evidence for Key Question 3.....	145
Table 26. Summary of evidence for Key Question 4.....	146

**FIGURES**

Figure 1. Flow chart showing results of literature search.....	60
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## APPENDICES

Appendix A. ALGORITHM FOR ARTICLE SELECTION .....	166
Appendix B. SEARCH STRATEGIES .....	167
Appendix C. EXCLUDED ARTICLES .....	169
Appendix D. LEVEL AND STRENGTH OF EVIDENCE DETERMINATION .....	170
Appendix E. LEVEL OF EVIDENCE FOR COMPARATIVE STUDIES .....	182
Appendix F. Summary of Manchikanti et al (2010) critical appraisal of the Chou et al (2009) APS evidence report .....	188
Appendix G. Chou's response to the Manchikanti et al (2010) critical appraisal of the Chou et al (2009) APS evidence report .....	191
Appendix H. Correspondence with Dr. Manchikanti regarding study methodology .....	198
Appendix I. Conflict of interest for Dr. Manchikanti (ASIPP and SIPMS) .....	202
Appendix J. Inclusion and exclusion criteria from RCTs: lumbar injections .....	203
Appendix K. Inclusion and exclusion criteria from RCTs: cervical injections .....	207
Appendix L. Efficacy data from RCTs: lumbar epidural injections .....	209
Appendix M. Efficacy data from RCTs: lumbar facet joint interventions .....	238
Appendix N. Efficacy data from RCTs: lumbar intradiscal injections .....	242
Appendix O. Efficacy data from RCTs: cervical epidural injections .....	244
Appendix P. Efficacy data from RCTs: cervical facet joint interventions .....	251
Appendix Q. Safety data from RCTs: lumbar spinal injections .....	255
Appendix R. Safety data from RCTs: cervical spinal injections .....	270
Appendix S. Safety data from non-randomized studies with $\geq 100$ patients. ....	276
Appendix T. Data from non-randomized studies designed to assess the incidence of vascular puncture. ....	290
Appendix U. Summary of the incidence of vascular puncture .....	295
Appendix V. Data from studies evaluating the cost-effectiveness of spinal injections. ....	297
Appendix W. CLINICAL PEER REVIEWERS .....	299

## EXECUTIVE SUMMARY

### Introduction

Although spinal injections have a long history of use for the treatment of chronic spinal pain and associated radiculopathies, questions remain regarding a number of important issues. When used in adult patients with chronic back or neck pain:

1. What is the evidence of efficacy and effectiveness of spinal injections?
2. What is the evidence of the safety of spinal injections?
3. What is the evidence that spinal injections have differential efficacy or safety issues in sub populations?
4. What is the evidence of cost implications and cost-effectiveness of spinal injections?

In light of the possible benefits of spinal injections, the potential impact of its use on health care costs and uncertainties regarding the evidence of effectiveness and safety in the short term and longer time horizons, patients, clinicians, and payers will benefit from a structured systematic appraisal of the comparative effectiveness, safety, and economic impact of spinal injections. Thus, the objective of this Health Technology Assessment is to critically appraise and analyze research evidence on the effectiveness of and complications related to the use of spinal injections in patients with chronic pain and to the extent possible, consider the potential financial impact.

### Methods for evaluating comparative effectiveness

Spectrum Research, Inc.'s (SRI) method for technology assessment involves formal, structured systematic search of the peer-reviewed literature across a number of databases in addition to searches of pertinent databases related to clinical guidelines and previously performed assessments. Each included study is critically appraised using SRI's Level of Evidence (LoE) system which evaluates the methodological quality based on study design as well as factors which may bias studies. An overall Strength of Evidence (SoE) combines the LoE with consideration of the number of studies and consistency of the findings to describe an overall confidence regarding the stability of estimates as further research is available. Included economic studies were also formally appraised based on criteria for quality of economic studies and pertinent epidemiological precepts.

Throughout the process, SRI sought clinical review to assure that the clinical components are accurately represented and relevant. In addition, peer-review by clinical experts, health services researchers and those with expertise in economic and outcomes evaluation provide an assessment of the systematic review methodology, analyses and report conclusions.

## Results/Summary

### Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?

Indication	Comparator	SoE	Conclusions/Comments
<b>Lumbar caudal or interlaminar epidural steroid injections:</b>			
<ul style="list-style-type: none"> <li>low back pain <u>with</u> sciatica or radiculopathy</li> </ul>	placebo	<b>Low*</b>	<ul style="list-style-type: none"> <li><b>In the short-term</b> (<math>\leq 3</math> months) there was <b>mixed evidence</b> based on data from twenty RCTs, seventeen of which were included in the Chou/APS SR<sup>39, 40</sup> (seven were considered to be higher-quality trials). Seven of seventeen studies included in the SR reported no benefit or inferior results while another seven reported positive results and three reported unclear results. Three LoE IIB RCTs published after the SR were added here, two reported on pain (both negative) and three on function (two negative and one positive) at three months.</li> <li><b>In the long-term</b> (<math>&gt; 3</math> months) there was <b>mixed evidence</b> based on data from twelve RCTs, nine of which were included in the Chou/APS SR<sup>39, 40</sup>. Seven of nine studies included in the SR reported no benefit or inferior results while positive results were reported by one study and another reported mixed results. Regarding the more recent RCTs included here, two reported on pain (both negative at twelve months, although one was positive at six months) and three on function (mixed results, one positive, one mixed, and one negative).</li> </ul>
<ul style="list-style-type: none"> <li>low back pain <u>without</u> sciatica or radiculopathy</li> </ul>	placebo	<b>Moderate*</b>	<ul style="list-style-type: none"> <li><b>no benefit</b> based on data from three RCTs, one of which was included in the Chou/APS SR and considered to be a lower-quality trial<sup>39, 40</sup>. In the two recent LoE IIB RCTs included here, there was no benefit in pain, function, or opioid use at three or in employment at twelve months.</li> </ul>
<ul style="list-style-type: none"> <li>spinal stenosis</li> </ul>	placebo	<b>Low* to moderate*</b>	<ul style="list-style-type: none"> <li><b>In the short-term</b> (24 hours – 3 months), there was <b>no benefit</b> based on data from four RCTs, three of which was included in the Chou/APS SR; one was considered to be a higher-quality trial<sup>39, 40</sup>. Three of four studies reported no benefit; one study reported improved walking distance at one week. In the one recent LoE IIB RCT included here, there was no benefit in pain, function, or opioid use at three months. (SoE = moderate)</li> <li><b>In the long-term</b> (13 – 30 months), there was <b>no benefit</b> based on data from two RCTs as reported in the Chou/APS SR<sup>39, 40</sup>. (SoE = low)</li> </ul>

Indication	Comparator	SoE	Conclusions/Comments
<ul style="list-style-type: none"> <li>failed back surgery syndrome</li> </ul>	placebo	<b>Moderate*</b>	<ul style="list-style-type: none"> <li><b>no benefit</b> based on data from three RCTs, two of which were included in the Chou/APS SR and considered to be lower-quality trials<sup>39, 40</sup>. In the one recent LoE IIb RCT included here, there was no benefit in pain, function, or opioid use at three months.</li> </ul>
<ul style="list-style-type: none"> <li>various</li> </ul>	adhesiolysis	<b>Low†</b>	<ul style="list-style-type: none"> <li><b>no benefit</b> based on data from five RCTs, three of which were included in the Chou/APS SR (one was considered higher-quality but with limitations)<sup>39, 40</sup>. In the two recent LoE IIb RCTs included here, there was no benefit in pain, function, or opioid use at three months. One study reported no benefit at twelve months as reported in the Chou/APS SR<sup>39, 40</sup>. <b>However</b>, three of the studies only enrolled patients who had who had previously failed epidural injections, and epidural injections served as the control, not as the intervention.</li> </ul>
<ul style="list-style-type: none"> <li>spinal stenosis</li> </ul>	physical therapy or control	<b>Very low*</b>	<ul style="list-style-type: none"> <li><b>no benefit</b> in terms of pain, function, or quality of life at three and six months based on data from one LoE IIb RCT.</li> </ul>
<ul style="list-style-type: none"> <li>sciatica and radiculopathy</li> </ul>	trigger point injection	<b>Low</b>	<ul style="list-style-type: none"> <li><u>In the short-term</u>, <b>epidural steroid injections were “modestly” superior</b> at three months based on data from one higher-quality RCT as reported in the Chou/APS SR<sup>39, 40</sup>. No long-term data were reported.</li> </ul>
<ul style="list-style-type: none"> <li>sciatica</li> </ul>	dry needling of the interspinous ligament	<b>Very low*</b>	<ul style="list-style-type: none"> <li><b>no benefit</b> based on data from one lower-quality RCT as reported in the Chou/APS SR<sup>39, 40</sup>. The length of follow-up was not reported.</li> </ul>
<ul style="list-style-type: none"> <li>low back pain with sciatica</li> </ul>	intramuscular steroid injections	<b>Low</b>	<ul style="list-style-type: none"> <li><b>no benefit</b> at two years based on data from one higher-quality RCT as reported in the Chou/APS SR<sup>39, 40</sup>. No short-term data were reported.</li> </ul>
<ul style="list-style-type: none"> <li>disc prolapse</li> </ul>	discectomy	<b>Low</b>	<ul style="list-style-type: none"> <li><b>no benefit (inferior)</b> in the short-term and up to two to three years based on data from one higher-quality RCT as reported in the Chou/APS SR<sup>39, 40</sup>.</li> </ul>
<b>Lumbar transforaminal epidural steroid injections:</b>			
<ul style="list-style-type: none"> <li>low back pain <u>with</u> sciatica or radiculopathy</li> </ul>	placebo	<b>Low*</b>	<ul style="list-style-type: none"> <li><b>mixed evidence</b> based on data from four RCTs, two of which were included in the Chou/APS SR and considered to be higher-quality<sup>39, 40</sup> and two of which were more recent LoE IIb studies. In terms of pain relief, the data suggest a benefit at two weeks (one study), mixed results at one month (two studies- one positive and one negative), and no benefit by 3 months. No benefit in function was reported at three months by two studies. Long-term data were mixed as reported by two higher-quality RCTs, both of which were reported in the Chou/APS SR<sup>39, 40</sup>, with one study reported positive results while the other showed no benefit.</li> </ul>

Indication	Comparator	SoE	Conclusions/Comments
• low back pain with sciatica or radiculopathy	intramuscular injection	Low	• <b>transforaminal steroid injections were superior to intramuscular injections</b> in terms of pain relief at one month based on data from one LoE IIb RCT.
• disc prolapse	oxygen-ozone ± steroids	Low*	• <b>no benefit</b> with no difference or inferior results at one week, three months, and six months based on data from two lower-quality RCTs as reported in the Chou/APS SR <sup>39, 40</sup> .
<b>Lumbar intraarticular facet joint steroid injections:</b>			
• confirmed or presumed facet joint pain	placebo	Low*	• <b>no benefit</b> in the first three months based on data from two RCTs included in the Chou/APS SR, one of which was considered to be lower-quality <sup>39, 40</sup> . Although one of the studies reported a statistically meaningful benefit at six months in patient improvement following steroid injection, the rationale for this late response is not clear.
• presumed facet joint pain	home stretching	Very low*	• <b>no benefit</b> in facet joint injections plus home stretching versus home stretching alone based on data from one lower-quality RCT included in the Chou/APS SR <sup>39, 40</sup> .
• non-radicular back pain and facet joint osteoarthritis	facet injections with hyaluronic acid	Low	• <b>no benefit</b> in the injection of steroids versus hyaluronic acid into the facet joint at six months based on data from one higher-quality RCT included in the Chou/APS SR <sup>39, 40</sup> .
<b>Lumbar medial branch blocks:</b>			
• confirmed facet joint pain	placebo	Very low*	• <b>no benefit</b> in terms of pain or function at both three and twelve months or on opioid use at twelve months based on data from one LoE IIb RCT.
• presumed facet joint pain	Sarapin	Low*	• <b>no benefit</b> in injections with Sarapin with or without steroid based on data from one higher-quality and one lower-quality RCT included in the Chou/APS SR <sup>39, 40</sup> .
<b>Lumbar sacroiliac joint steroid injections:</b>			
• sacroiliac joint pain	placebo	Low	• <b>sacroiliac joint injections were superior</b> to placebo injections based on data from one higher-quality RCT included in the Chou/APS SR <sup>39, 40</sup> .
<b>Lumbar intradiscal steroid injections:</b>			
• discogenic back pain	placebo	Moderate*	• <b>no benefit</b> based on data from three RCTs included in the Chou/APS SR, one of which was higher-quality <sup>39, 40</sup> .
• sciatica	chemo-	Moderate*	• <b>no benefit</b> based on data from three RCTs included in

Indication	Comparator	SoE	Conclusions/Comments
	nucleolysis		the Chou/APS SR, one of which was higher-quality <sup>39, 40</sup> .
<b>Lumbar intradiscal injections with neurolytic agent:</b>			
• low back pain without radiculopathy	placebo	<b>Low</b>	• <b>intradiscal injections with methylene blue were superior</b> to placebo injections in terms of pain, function, patient satisfaction, and analgesic use in the long-term (6-24 months) based on data from one LoE IIa RCT.
<b>Cervical epidural steroid injections:</b>			
• neck pain <u>with</u> disc herniation and radiculitis	placebo	<b>Very low*</b>	• <b>no benefit</b> in terms of pain, function, or opioid use at both three and twelve months or on employment at twelve months based on data from one LoE IIb RCT.
• neck pain <u>without</u> disc herniation and radiculitis	placebo	<b>Very low*</b>	• <b>no benefit</b> in terms of pain, function, or opioid use at both three and twelve months or on employment at twelve months based on data from one LoE IIb RCT.
• neck pain with disc compression and radiculitis	intramuscular injection	<b>Very low*</b>	• <b>epidural injections were superior</b> to intramuscular injections in the posterior neck in terms of pain, analgesic use, and employment at one week and twelve months based on data from one LoE IIb RCT.
<b>Cervical intraarticular facet joint steroid injections:</b>			
• confirmed facet joint pain	placebo	<b>Very low*</b>	• <b>no benefit</b> in terms of the length of pain relief based on data from one LoE IIb RCT. No long-term data was reported.
<b>Cervical medial branch blocks:</b>			
• confirmed facet joint pain	placebo	<b>Very low*</b>	• <b>no benefit</b> in terms of pain or function at both three and twelve months or on opioid use or employment at twelve months based on data from one LoE IIb RCT.

NA: not applicable

\* Overall strength of evidence rating was downgraded one level due to limitations in study design or execution.

† Overall strength of evidence rating was downgraded two levels as at least two of the three trials had serious limitations in their design: inclusion criteria limited enrollment to patients who had previously failed epidural injections and epidural injections had served as the control treatment.

## Key Question 2: What is the evidence of the safety of spinal injections?

Spinal injections	Strength of evidence	Conclusions/Comments
<ul style="list-style-type: none"> <li>Major complications</li> </ul>	High	<ul style="list-style-type: none"> <li><b>Major complications are rare</b> following injections into the lumbar or cervical spine. There were no cases of death or paralysis in the included studies, although there have been case reports of each in the published literature.</li> <li><b>Lumbar injections:</b> In 14 recent RCTs, there were reports of dural puncture, subarachnoid puncture, and angina pectoris in 1/1556 injections or patients (each). In six case series there was one case each of dural puncture and subarachnoid puncture (1/10,416 injections or patients (each)). No deaths were attributed to spinal injection procedures; death unrelated to the procedure occurred in 10/1146 patients in the RCTs. Chou reported in the APS SR<sup>39, 40</sup> that major complications were rare but inadequately reported in trials of lumbar epidural steroid injections, and noted one case of dural puncture.</li> <li><b>Cervical injections:</b> In five RCTs, there were reports of subarachnoid puncture in 3/710 injections or patients and no reports of dural puncture or death. In four case series there were reports of life-threatening generalized anaphylactic reaction (1 case), grand-mal seizure (1 case), dural puncture (2 cases), and local hematoma (1 case) in 7240 injections or patients.</li> </ul> <p>In three case reports of a <u>mix of lumbar and cervical spinal injection patients</u>, there was one case of each of the following major complications in 6935 injections: chest pain, tachycardia/hypertension, significant transient hypertensive episode, hematoma, dural puncture, and a severe vasovagal reaction.</p>
<ul style="list-style-type: none"> <li>Minor complications</li> </ul>	High	<ul style="list-style-type: none"> <li><b>Minor complications are more common but are generally transient in nature.</b> The overall minor complication rate ranged from 0.06% to 16.3% of injections or patients in 19 RCTs and 14 case series, and complications included: pain at the injection site, increased radicular pain/numbness/weakness, nerve root irritation, superficial infections, sympathetic blockade, facial flushing, vasovagal reactions/fainting, headache, gastric complaints, dizziness, pruritis, irregular periods, and insomnia.</li> </ul>
<ul style="list-style-type: none"> <li>Vascular puncture</li> </ul>	Low	<ul style="list-style-type: none"> <li><b>The mean incidence of intravascular puncture following fluoroscopically guided lumbar spinal injections was 10.18%</b> (range, 1.9–22%) as reported in five case series designed to assess its incidence. These studies evaluated the incidence but not the consequences of intravascular injection.</li> </ul>
<ul style="list-style-type: none"> <li>Radiation exposure to the physician</li> </ul>	Low	<ul style="list-style-type: none"> <li><b>With proper protective measures, total radiation exposure was within normal limits</b> following a mean of 923 procedures (range, 100 – 1819) with an average length of radiation exposure of 9.8 seconds/procedure (range, 4.9 – 15.2) in all five case series we identified.</li> </ul>

### Key Question 3: What is the evidence that spinal injections have differential efficacy or safety issues in sub populations?

Spinal injections	Strength of evidence	Conclusions/Comments
<b>Lumbar Epidural Steroid Injection</b>		
• Approach of epidural steroid injection	<b>Low*</b>	• There is <b>no consistent evidence</b> from a systematic review of six RCTs and two additional RCTs published since the systematic review that one approach is more efficacious in administering lumbar epidural steroid. The results of one lower quality RCT suggest that interlaminar injections may not be as efficacious as transforaminal in patients with axial only pain from spinal stenosis. However, more study is needed to verify these findings.
• Diagnosis	<b>Very low</b>	• There is <b>no consistent evidence</b> that epidural steroid injections have differential efficacy or effectiveness among various diagnoses of the lumbar or cervical spine.
• Pre-injection pain intensity or duration, type of steroid, sex, age, or MRI findings	<b>Very low</b>	• There is <b>no consistent evidence</b> that pre-injection pain intensity or duration, type of steroid used as injectate, sex, age or pre-injection MRI findings are associated with outcome in patients receiving epidural steroid injections of the lumbar or cervical spine.

NA: not applicable

\* Overall strength of evidence rating was downgraded one level due to limitations in study design or execution.

### Key Question 4: What is the evidence of cost implications and cost-effectiveness of spinal injections?

	Strength of evidence	Conclusions/Comments
• Economic analysis	<b>Very low</b>	<ul style="list-style-type: none"> <li>▪ <b>There is no evidence that epidural steroid injections are cost effective</b> based on data from two economic analyses. One moderately well conducted cost utility analysis (QHES 78/100) suggested that one epidural steroid injection is a more cost effective patient management strategy than up to three injections and that cost effectiveness ratios for epidural steroid injections are too high to be considered cost effective by UK conventions. Further, the budget impact of epidural spinal injections is likely large because of high use. Poor economic data (QHES 49/100) from a second trial (Karppinen) suggested that over one year epidural steroid injections do not show cost or outcome advantages compared to saline injections, and that contained herniations may be more responsive to steroid injection than bulges or extrusions.</li> <li>▪ No economic data were available for facet injections, medial branch blocks, sacroiliac joint injections, or intradiscal injections or for any type of cervical injection.</li> </ul>

# 1. Appraisal

## 1.1. *Rationale*

It is estimated that up to 75% of the population has had an episode of back pain at some point in their life<sup>13</sup>. While most acute back pain resolves within a few months, surveys report that approximately 5% of the population has chronic back pain<sup>13</sup>, a percentage which implicates significant social and economic impacts. The risk of spinal pain increases with age as a result of disc disease and spinal degeneration<sup>150</sup>. Those affected can have disabling symptoms that can dramatically affect their quality of life and ability to perform a variety of activities<sup>213</sup>. Chronic spinal pain can be attributed to a number of pathologies, including (but not limited to) degenerative disc disease (DDD), herniated nucleus pulposus (HNP) (or herniated/slipped disc), spinal stenosis, radiculopathy, failed back surgery syndrome (FBSS), facet joint syndrome, and whiplash.

Treatment for chronic back pain typically begins with the identification of the underlying cause of pain and follows with conventional medical management (CMM), which varies with the diagnosis. CMM may include conservative/ non-invasive interventions such as physical therapy and rehabilitation, pharmaceutical pain management, psychological therapy and coping skills, exercise, education, antidepressants, cognitive behavioral therapy and supported self-management, spinal manipulation, electrical stimulation, injections outside the spine, implanted devices, acupuncture/acupressure, and modified work<sup>6</sup>.

Patients who don't respond to non-invasive treatment are typically referred for more invasive and non-surgical therapies such as spinal injections in an attempt to provide pain relief. Spinal injections involve the injection of an anti-inflammatory agent such as a steroid and/or an anesthetic into the spine or space around the spinal nerves and joints. One of the theoretical advantages of spinal injections is that they deliver the treatment medication directly to the site involved in the source of pain<sup>81</sup>. Types of spinal injection include epidural, facet joint, intradiscal, and sacroiliac joint injections. Spinal injections can be used for diagnostic and therapeutic purposes. According to one study examining Medicare claims of lumbosacral injections, the number of epidural steroidal injections increased 271% and the number of facet injections increased 231% from 1994 to 2001<sup>51</sup>. A similar study found that lumbar facet joint injections/diagnostic blocks increased 161% from 2002 to 2006<sup>130</sup>.

Significant questions remain about the efficacy and effectiveness (particularly long term), safety, and the cost effectiveness of spinal injections.

## 1.2. Key Questions

Key questions are developed by the Washington State Health Technology Assessment Program.

**When used in adult patients with chronic back or neck pain:**

### Key Question 1:

What is the evidence of efficacy and effectiveness of spinal injections? Including consideration of:

- a. Short-term and long-term measures, including measures related to:
  - repeated spinal injections
  - multilevel spinal injections
  - bilateral versus unilateral spinal injections
- b. Impact on clinically meaningful physical function and pain
- c. Impact on quality of life, patient satisfaction
- d. Opioid use, return to work, and any other reported surrogate measures

### Key Question 2:

What is the evidence of the safety of spinal injections? Including:

- a. Adverse event type and frequency (mortality, major morbidity, other)
- b. Dural or arachnoid puncture
- c. Infection
- d. Epidural or intradural hematoma
- e. Allergic reaction
- f. Nerve or spinal cord injury
- g. Artery/vein damage/puncture
- h. Arachnoiditis

### Key Question 3:

What is the evidence that spinal injections have differential efficacy or safety issues in sub populations? Including consideration of:

- a. Gender
- b. Age
- c. Psychological or psychosocial co-morbidities
- d. Diagnosis or time elapsed from fracture
- e. Other patient characteristics or evidence based on patient selection criteria
- f. Provider type, setting, or other provider characteristics
- g. Payer/ beneficiary type: including worker's compensation, Medicaid, state employees

### Key Question 4:

What is the evidence of cost implications and cost-effectiveness of spinal injections?

Including:

- a. Direct costs over short term and over expected duration of effect
- b. Comparative costs

### 1.3. Outcomes Assessed

The studies included in this assessment used a variety of measures to evaluate treatment outcomes, which are outlined in Table 1. The 10-cm visual analogue scale (VAS) was the most commonly used tool for assessing pain intensity and pain relief. Visual pain scales are used in studies of pain treatment as a tool for quantifying pain relief or improvement between pre- and post-treatment measurements; the changes in pain intensity are compared between treatment groups.

**Table 1. Outcome measures**

Outcome measure	Clinician or patient reported	Instrument type	Components	Score range	Interpretation
Nottingham Health Profile <sup>87</sup>	Patient	Generic	Physical mobility Pain Sleep Emotional reactions Social isolation Energy level	0–100	Higher scores = lower function
ODI (Oswestry Disability Index, or Oswestry Low Back Pain Disability Questionnaire) (version 2.0) <sup>55</sup>	Patient	Back	Pain intensity Personal care Lifting Walking Sitting Standing Sleeping Sex life Social life Travelling	0–100*	Higher scores = greater disability
Roland-Morris Disability Questionnaire (RDQ) <sup>171</sup>	Patient	Back	Pain intensity Self care Social life Walking Sitting Standing Sleeping Bending Stairs Appetite General activity Household chores	0–24	Higher scores = greater disability
VAS pain (Visual Analogue Scale)	Patient	Generic	Pain	0–10 cm or 0–100 mm	No pain: 0 Worst pain imaginable: 10
NRS (Numerical Rating System) <sup>141, 212</sup>	Patient	Generic	Pain	0 – 10	No pain: 0 Mild pain: 1 – 3 Moderate pain: 4 – 6 Severe pain: 7 – 10
NDI (Neck Disability Index) <sup>37, 207</sup>	Patient	Neck	Pain intensity Personal care Lifting Reading Headaches Concentration	0 – 50 or 0 – 100*	Higher scores = greater disability

			Work Driving Sleeping Recreation		
SCL (Symptom Checklist) <sup>19, 50</sup>	Patient	Generic	Somatization Obsessive-compulsive Interpersonal sensitivity Depression Anxiety Hostility Phobic anxiety Paranoid ideation Psychotic tendency	0 - 4	Not at all distressed: 0 Extremely distressed: 4
MPQ (McGill Pain Questionnaire) <sup>147</sup>	Patient	Generic	Sensory Affective Evaluative	0 – 78	Higher scores = greater pain
Faces Pain Scale	Patient (children)	Generic	Pain	0 – 5	Higher scores = greater pain
LBOS (Low Back Outcome Score) <sup>73</sup>	Patient	Low back	Current pain using VAS Employment Domestic chores or "odd jobs" Sports or active social activities Resting Treatment/consultation with health care provider Analgesia use Sex life Sleeping Walking Sitting Traveling Dressing	0 – 75	Poor: 0 – 29 Fair: 30 – 49 Good: 50 – 64 Excellent: ≥ 64

\* ODI and NDI: Each of the ten subscales is scored on a scale of 0–5 points; the total score is then doubled for a final score ranging from 0–100 points.

## 2. Background

### 2.1. *The condition*

It is estimated that 75–80% of the population has had an episode of back pain at some point in their life<sup>13</sup>. While most acute back pain resolves within a few months, surveys report that approximately 5-10% of the population has chronic back pain<sup>13, 58</sup>, a percentage which may be rising<sup>58</sup> and implicates significant social and economic impacts. Chronic back pain is defined as pain that persists for more than three months and most commonly occurs in the lumbar or cervical area. Those affected can have disabling symptoms that can dramatically affect their quality of life and ability to perform a variety of activities<sup>213</sup>. While lumbar pain affects both sexes equally, cervical pain is more common in females<sup>47</sup>. The risk of spinal pain increases with age as a result of disc disease and spinal degeneration<sup>150</sup>. Other risk factors include poor posture, anxiety or depression, and accidents or occupational injuries.

Chronic spinal pain can be attributed to a number of pathologies, including:

- **Degenerative disc disease (DDD)** is a term used to describe any number of changes that may occur as a normal part of the aging process. Degenerative changes include loss of fluid from the discs, making the discs thinner and inflexible and compressing the discs; cracks or tears in the disc may also occur and could lead to slipped or bulging discs. While some people are not affected by these changes, others experience pain as a result of spinal cord or nerve compression. DDD occurs most often in the cervical or lumbar spinal regions and in those who are obese, smokers, or perform heavy physical work<sup>214</sup>.
- **Herniated nucleus pulposus (HNP)**, also known as a herniated or slipped disc, occurs when a tear or weakening occurs in the outer portion of a disc, allowing the central portion (nucleus pulposus) to bulge out and press on the surrounding nerves<sup>146</sup>. Herniated discs are more common in the lumbar region and in middle-aged and older men, especially accompanying strenuous physical activity.
- **Spinal stenosis** is defined as the narrowing of the spinal canal, causing pressure on the spinal cord or nerves and occurs most often in the lumbar region<sup>5</sup>. People at higher risk for spinal stenosis include those over 50 years old, females, and those with a history of spinal injury or surgery.
- **Radiculopathy** is any disease affecting the nerve roots in the cervical or lumbar region, causing sharp pain or numbness in the arms or legs<sup>4, 184</sup>. Causes of radiculopathy include disc herniation, spinal stenosis, and osteoarthritis. Related conditions are:
  - Radiculitis - an inflammation of a spinal nerve root, causing radicular pain<sup>187</sup>
  - Sciatica - pain or numbness in a leg that may or may not have its origins in the back<sup>184</sup>
  - Cervicobrachialgia - pain in the neck radiating down the arm.

- **Failed back surgery syndrome (FBSS)**, also known as post surgery syndrome, is a general term denoting persistent or recurrent chronic lower back or leg pain following what appears to have been anatomically successful spinal surgery<sup>91, 204</sup>. It is estimated to affect 10 to 40% of patients following lumbar spine surgery<sup>91, 100, 154</sup>. Treating FBSS patients is challenging, as additional surgery and conservative therapies typically do not relieve pain<sup>204</sup>.
- **Facet joint syndrome** is pain occurring in the facet joints (known formally as zygapophysial or Z joints<sup>20</sup>) and most often affects the lower back and neck<sup>44</sup>. Facet joint pain occurs most often in the elderly, accompanying the degeneration of the cartilage covering the facet joints. Irritation of the facet joint nerves, trauma, inflammation, and disc degeneration are also associated with facet joint pain.
- **Whiplash** describes an extension/flexion injury occurring as the result of a vehicle accident, most often a rear-end collision<sup>188, 189, 194</sup>. There are a variety of resulting conditions including joint dysfunction, disc herniation, chronic pain, faulty muscle movement, and cognitive or mental function problems. Females are more frequently and more seriously affected by whiplash<sup>189</sup>; advanced age and pre-existing health conditions such as arthritis can also increase the severity of the condition.

## 2.2. *The technology and its comparators*

### *Comparators*

Treatment for chronic back pain typically begins with the identification of the underlying cause of pain, which remains challenging because the pathogenesis and mechanisms for the majority of chronic back pain remain unknown.<sup>13</sup> Depending upon the diagnosis, a variety of treatments can be administered. These treatments, which are collectively referred to as conventional medical management (CMM) include conservative/ non-invasive interventions such as physical therapy and rehabilitation, pharmaceutical pain management, psychological therapy and coping skills, exercise, education, antidepressants, cognitive behavioral therapy and supported self-management, spinal manipulation, electrical stimulation, injections outside the spine, implanted devices, acupuncture/acupressure, and modified work<sup>6</sup>. Spinal injections are not usually performed until these less invasive treatments have been tried and have not provided adequate relief.

### *Spinal injections*

Patients who don't respond to non-invasive treatment are typically referred for more invasive and non-surgical therapies such as spinal injections in an attempt to provide pain relief. Spinal injections involve the injection of an anti-inflammatory agent such as a steroid and/or an anesthetic into the spine or space around the spinal nerves and joints. One of the theoretical advantages of spinal injections is that they deliver the treatment medication directly to the site involved in the source of pain<sup>81</sup>. Fluoroscopic or computed tomography (CT) visualization is often used to improve the accuracy of medication delivery. Types of spinal injection include epidural, facet joint, intradiscal, and sacroiliac joint injections. Spinal

injections can be used for diagnostic and therapeutic purposes. According to one study examining Medicare claims of lumbosacral injections, the number of epidural steroidal injections increased 271% and the number of facet injections increased 231% from 1994 to 2001<sup>51</sup>. A similar study found that lumbar facet joint injections/diagnostic blocks increased 161% from 2002 to 2006<sup>130</sup>.

### 2.3. *Mechanism of action*

Corticosteroids administered for therapeutic spinal pain relief work in several ways. They stabilize membranes; inhibit the synthesis or action of neural peptides; inhibit the synthesis or release of inflammatory substances, including phospholipase A<sub>2</sub>, arachidonic acid and its metabolites, tumor necrosis factor alpha, interleukin 1, and prostaglandin E<sub>2</sub>; suppress the sensitization of dorsal horn neurons; and suppress ongoing neuronal discharge<sup>81, 144</sup>. In the case of radiculopathy, glucocorticoids relieve both the early and late effects of inflammation<sup>144</sup>. For patients with referred back pain from degenerative disc disease, the corticosteroids likely work by reducing impulses from the posterior longitudinal ligament and the outer annulus of the intervertebral disc<sup>144</sup>.

The anesthetic administered for both diagnostic and therapeutic use works by dampening C-fiber activity and interrupting the nociceptive input and reflex mechanisms of the afferent limb of local pain fibers, interrupting the pain-spasm cycle<sup>81</sup>. It has also been theorized that the anesthetic acts on the free glutamate released by herniated disc material and clears adhesions or inflammatory exudates from the affected neural structure<sup>81</sup>.

### 2.4. *Injection procedures*

In general, spinal injections deliver a combination of medications (a corticosteroid and an anesthetic) into the affected area after the patient receives an injection of a local anesthetic to numb the skin.

**Epidural injections** deliver medication into the epidural space of the spine to decrease inflammation of the nerve root<sup>139</sup>. Three approaches are possible, depending on the location and source of pain and on the physician's preference and experience<sup>144</sup>. The interlaminar or translaminar approach involves placement of the needle between the lamina of the vertebrae, delivering medication to both the right and left sides of the inflamed area<sup>139</sup>. The transforaminal approach involves placement of the needle in the neural foramen, treating one side at a time. The caudal lumbar approach is performed via the sacral hiatus<sup>186</sup>. Caudal and interlaminar/translaminar injections have been traditionally used, but transforaminal injections are gaining in popularity, particularly in treating unilateral radiculopathy<sup>144</sup>. The caudal approach is considered to be less demanding and has a lower risk of intradural injection, but requires larger volumes of injectate. The interlaminar/translaminar approach requires significant dexterity for accurate treatment<sup>185</sup>, yet requires less medication than the caudal approach and has a lower risk of damaging the nerve root<sup>144</sup>. The transforaminal approach offers a closer delivery of the medication to the nerve root compared with the

interlaminar approach, allowing the use of lower doses of medication. This approach is particularly useful in treating large disk or lateral disk herniations and foraminal stenosis, but has a higher risk of damaging the nerve root.

**Facet joint injections** deliver the medications (anesthetic with or without a corticosteroid) into the facet joints and include several approaches. Medial branch blocks involve injection of the medication into the area of the medial branch of the posterior primary ramus<sup>6, 20, 140</sup>. Intraarticular injections involve an injection into the facet (zygapophysial) joints. Prior to steroid injections, controlled diagnostic blocks of the joint or the nerves that supply the joint are often performed using local anesthetic<sup>22</sup>. A positive block indicates that pain is eliminated and the affected nerve has been identified as the source of pain.<sup>20, 40, 48</sup> There is some controversy as to the amount of pain relief that constitutes a positive response, varying from 50% to 100%<sup>20</sup>. Repeated blocks with anesthetics of different duration of action can verify the exact location of facet joint pain, but must be done in a controlled manner to be valid. For therapeutic and diagnostic purposes, the choice between a medial branch block and intraarticular injection is somewhat dependent on the physician's preference and training. Intraarticular injections carry the risk of leakage of fluid into the epidural space and nerve roots, are more difficult to perform, especially if age-related changes or trauma cause difficulty entering the facet joint, and are more time consuming<sup>22</sup>. The procedure for medial branch blocks can be performed more efficiently and with a lower dose of corticosteroids.

**Intradiscal injections** deliver steroids directly into the intervertebral disc<sup>6</sup> and can be used for both diagnostic and therapeutic purposes. Intradiscal injections of steroids are thought to promote stabilization by causing a contraction of the disc tissue and suppressing inflammation within the disc<sup>149</sup>. Risks of the procedure seem to be minimal, but this remains a controversial topic<sup>149</sup>.

Diagnostic and therapeutic **sacroiliac joint injections** deliver local anesthetic and/or corticosteroids into or around the sacroiliac joint<sup>6</sup>. The use of this type of injection in patients without spondylarthropathy remains controversial<sup>40</sup>. A positive response from a diagnostic injection is poorly defined and dependent upon individual physician preferences<sup>77</sup>. A positive diagnostic block can identify either sacroiliac joint structures or joint malfunction as a potential source of pain<sup>22, 77</sup>. Diagnostic sacroiliac joint blocks can be among the most challenging of spinal injection procedures, with false-positive and false-negative blocks possible<sup>77</sup>.

Approximately 50% of four million interventional medical procedures per year are performed under fluoroscopic guidance<sup>120</sup>. Fluoroscopy for spinal injections is routinely used to ensure correct needle placement, accurate delivery of the injectate, and avoidance of complications. Incorrect needle placement during spinal injections without the use of fluoroscopy has been reported by various studies in 12.5% to 38.3% of patients<sup>24</sup>. A C-arm fluoroscope allows the X-ray tube to be moved around the prone patient and an image intensifier enhances the image, making it easier to interpret<sup>27</sup>. Although studies have shown that radiation exposure to physicians using fluoroscopy for spinal injections is within safety limits<sup>24, 27, 119-121</sup>, other methods, including ultrasound and CT, are being investigated as non-radioactive or lower radioactive methods of needle guidance.

## 2.5. *Indications*

In general, epidural, facet joint, and sacroiliac joint injections are indicated for average pain levels greater than 6 on scale of 0 – 10; intermittent or continuous pain causing functional disability; or chronic pain that has failed to respond to more conservative therapies<sup>114, 144</sup>.

- **Lumbar transforaminal injections** are indicated in patients with chronic low back and/or lower extremity pain resulting from disc herniation, FBSS without extensive scar tissue and hardware, spinal stenosis with radiculitis, or discogenic pain with radiculitis<sup>59, 114, 144</sup>.
- **Lumbar interlaminar and caudal epidural injections** are indicated in patients with disc herniation/lumbar radiculitis; lumbar spinal stenosis; post lumbar surgery syndrome; epidural fibrosis; degenerative disc disease/discogenic low back pain; and negative for facet joint pain<sup>59, 114, 144</sup>.
- **Cervical interlaminar epidural injections** are indicated in patients with a herniated, protruded, or extruded disc with or without radiculitis; cervical spinal stenosis; post cervical surgery syndrome; degenerative disc disease; and negative for facet joint pain<sup>114</sup>.
- **Lumbar or cervical facet joint blocks** are indicated in patients with chronic somatic or non-radicular low back/cervical pain or headache and lower/upper extremity pain; no evidence of either discogenic or sacroiliac joint pain; no evidence of disc herniation or radiculitis; inability to undergo physical or chiropractic therapy; inability to tolerate non-steroidal anti-inflammatory medications<sup>114</sup>. Therapeutic facet joint nerve blocks are indicated in patients with a positive response (80% relief) to a controlled anesthetic block<sup>114</sup>.
- An **intradiscal injection** is indicated in patients with internal disc disruption with Modic changes on an MRI and signs of end-plate inflammatory changes<sup>149</sup>, chronic discogenic low back pain,<sup>39</sup> and lumbar disc prolapse with sciatica or radiculopathy<sup>39</sup>.
- **Sacroiliac joint injections** are indicated in patients with chronic somatic or nonradicular low back and lower extremity pain that is greatest below the level of L5, and lack of evidence for disc-related or facet joint pain<sup>114</sup>. A therapeutic sacroiliac joint injection is indicated with a positive sacroiliac diagnostic block of at least 80% pain relief<sup>114</sup>.

## 2.6. *Contraindications*

Spinal injections are not indicated in patients with a history of allergy to any of the medications used<sup>20, 114</sup>. Lumbar epidural injections are not indicated for uncompensated coagulopathy including bleeding disorders; ongoing use of anticoagulant medications; infection; diabetes mellitus, prominent motor deficit or paresis suggestive of severe root or cauda equina compression; failure of previous injections to provide benefit; severe spinal stenosis as demonstrated by imaging studies; local malignancy; and acute spinal cord compression<sup>59, 144</sup>. In addition, some factors that can negatively affect the outcome include smoking, chronic pain syndrome, axial-only pain or diffuse pain, opioid dependence, and disability claims<sup>144</sup>.

## 2.7. *Potential Complications and Harms*

Complications of the various types of spinal injections can arise from the procedure itself or from any of the injectates used, and may include<sup>1, 14, 17, 22, 34, 45, 59, 71, 77, 81, 92, 112, 114, 123, 144, 152</sup>:

- **Major and minor procedural complications** including infection; hematoma; intravascular uptake; nerve damage; dural puncture (possibly resulting in a headache); unintentional subarachnoid, intrathecal, or subdural injection; disc entry; permanent spinal cord injury; air embolism; pneumocephalus; brain/spinal cord infarction; brain/spinal cord edema; intracranial hypotension; retinal hemorrhage or cortical blindness; transient neurologic deficits; vasovagal syncope; arachnoiditis; myelopathy/cauda equina syndrome; local discomfort or swelling; increased general or radicular pain; bleeding, especially if the patient is on anticoagulant therapy; urinary complications; epidural granuloma; abscess; death; and radiation exposure.
- **Complications from the corticosteroids** include suppression of the hypothalamic-pituitary axis; elevation of blood sugar in diabetics; elevated blood pressure; fluid retention in patients with congestive heart failure; dizziness; nausea/vomiting; weakness; headache; tachycardia; facial erythema; transient hypotension/hypertension; gastritis; mood swings; pruritus; insomnia; menstrual irregularities; Cushingoid syndrome; meningitis; and electrolyte imbalance.
- **Complications related to any of the injectates or additives** include allergic reactions; facial flushing; high spinal anesthesia; and hypersensitivity or anaphylactoid reactions.
- **Other possible complications** include seizure; transient global amnesia; organic brain syndrome; and muscle spasm.

## 2.8. Clinical Guidelines

### National Guideline Clearinghouse

A search of the National Guidelines Clearinghouse for spinal injection retrieved 15 potential guidelines, 11 of which provided specific guidance for the use of spinal injections. We identified three additional guidelines. All 14 guidelines are summarized in reverse chronological order below:

#### **American Pain Society (APS) (2009)<sup>41</sup>:**

*Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain (Chou et al)*

For patients with nonradicular low back pain, the APS is unable assess the benefit of epidural steroid injection, facet joint steroid injection, medial branch block, or sacroiliac joint injection based on insufficient or poor evidence (Grade I). Corticosteroid facet joint injection is not recommended based on moderate evidence. Intradiscal steroid injection is not recommended for treatment of nonradicular low back pain based on good evidence (Grade D).

For patients with radicular low back pain, the APS found moderate evidence for short-term (through three months) benefit from epidural steroid injections based on fair evidence (Grade B). Physicians should discuss the risks and benefits of epidural steroid injection, and such discussions should include the lack of evidence for long-term benefit of epidural steroid injections.

A recommendation for epidural steroid injection for patients with symptomatic spinal stenosis is not offered based on insufficient or poor evidence (Grade I). Intradiscal steroid injection was not found to be more effective than chemonucleolysis for patients with symptomatic spinal stenosis, and no recommendation is given (Grade C).

#### **American Society of Interventional Pain Physicians (2009)<sup>114</sup>:**

*Comprehensive evidence-based guidelines for interventional techniques in the management of chronic spinal pain (NGC:007428)*

The recommendation for caudal epidural steroid injection in managing lumbar spinal pain with disc herniation and radiculitis or discogenic pain without disc herniation or radiculitis is 1A or 1B, indicating a strong recommendation where the benefits outweigh the risks of treatment. In addition, the recommendation for caudal epidural steroid injection for patients with post-lumbar laminectomy syndrome and spinal stenosis is 1B or 1C, also indicating a strong recommendation. The recommendation for use of cervical interlaminar epidural injection for disc herniation and radiculitis to achieve short-term relief is 1C. For patients seeking long-term relief, the recommendation is 2B (weak recommendation), indicating benefits are balanced with risks and burdens of treatment. In patients with spinal stenosis and discogenic pain without disc herniation and radiculitis the recommendation is 2C (very weak, with uncertainty in estimates of benefits, risk, and burden of treatment). The recommendation

for lumbar transforaminal epidural injections is 1C. Intraarticular facet joint injections are not recommended. Cervical, thoracic, and lumbar facet joint nerve blocks are recommended to provide both short-term and long-term relief in the treatment of chronic facet joint pain (recommendation 1B or 1C).

**Institute for Clinical Systems Improvement (2009):**

*Assessment and management of chronic pain (NGC:007602)*

Epidural steroid injections and facet joint injections are classified as level I (standard, first-line) therapeutic procedures, and are recommended as part of a comprehensive treatment plan that includes pharmacologic, rehabilitative, and psychological interventions. Evidence is limited when such procedures are used alone.

**American College of Occupational and Environmental Medicine (2008):**

*Chronic pain NGC:007160*

Epidural glucocorticosteroid injection is recommended as a treatment option for subacute radicular pain syndromes, and as an option for second-line treatment of acute flare-ups of spinal stenosis associated with true radicular or radiculomyelopathic symptoms based on low potential harm to the patient and low costs (Evidence Rating I: insufficient evidence).

Epidural glucocorticosteroid injection is not recommended to treat chronic neck pain or for dorsal spine symptoms that predominate over leg pain based on evidence that harms and cost exceed benefits to the patient (Evidence Rating C: limited evidence).

The ACOEM makes no recommendation regarding the use of facet joint injection for flare-ups of neuropathic pain or chronic low back pain (Evidence Rating I: insufficient evidence).

Facet joint injection is not recommended for any radicular pain syndrome, chronic non-specific axial pain, and repeat injections are not recommended for patients who failed to achieve lasting functional improvements after a prior injection for neuropathic or chronic low back pain based on evidence that treatment is ineffective or that costs or harms outweigh benefits to the patient (Evidence Rating B: moderate evidence).

**Institute for Clinical Systems Improvement (2008):**

*Adult low back pain (NGC:006888)*

ICSI recommends epidural steroid injection only after conservative treatment has failed and to avoid surgical intervention. ICSI finds limited evidence for the efficacy of epidural steroid injection, but indicates it may allow patients to progress with conservative treatments.

Epidural steroid injection should be performed under fluoroscopy with contrast in order to prevent treatment failure.

**Work Loss Data Institute (2008):**

*Low back - lumbar & thoracic (acute & chronic) (NGC:006562)*

Epidural steroid injection and sacroiliac joint injections are recommended as part of a comprehensive treatment plan for low back pain. Specifically, epidural steroid injection is recommended to avoid surgery for severe cases with radiculopathy, but does not offer long-term functional benefit. "Series of three" epidural steroid injections, facet joint injection (multiple series, thoracic, and medical branch blocks), and intradiscal steroid injection were considered but are not recommended.

**Work Loss Data Institute (2008):**

*Neck and upper back (acute & chronic) (NGC:006563)*

Epidural steroid injection is recommended as part of a comprehensive treatment plan for radicular pain. Specifically, epidural steroid injection is recommended to avoid surgery in severe cases with neurologic findings. Facet joint injection was considered but is not recommended.

**Work Loss Data Institute (2008):**

*Pain (chronic) (NGC:006564)*

Epidural steroid injection is recommended as part of a comprehensive treatment plan. Facet blocks are classified as under study by the Institute and are not currently recommended.

**American Academy of Neurology (2007):**

*Assessment: use of epidural steroid injections to treat radicular lumbosacral pain. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (NGC:005580)*

The American Academy of Neurology indicates the use of epidural steroid injections may result in a small magnitude of improvement in radicular lumbosacral pain when evaluated 2-6 weeks post-injection, but the recommendation is classified as a level C (possibly effective) due the small number of relevant studies, highly select patient population, and variation in comparison treatments in the evidence base.

Epidural steroid injections are not recommended for radicular lumbosacral pain due to a lack of evidence for improvement of function, need for surgery or long-term pain relief beyond 3 months. This recommendation is classified as level B (probably ineffective based on Class I-III evidence).

There was insufficient evidence to make a recommendation regarding the use of epidural steroid injections to treat cervical radicular pain.

**American College of Occupational and Environmental Medicine (2007):**

*Low back disorders (NGC:006456)*

The use of epidural glucocorticosteroid injection is recommended as a second-line treatment of acute spinal stenosis flare-ups, and as a treatment option for acute or subacute radicular pain syndromes lasting at least 3 weeks after treatment with NSAIDs and when pain is not trending towards spontaneous resolution. Both treatments are recommended based on low potential harm to the patient and low costs (Evidence Rating I: insufficient evidence).

The use of facet joint injections is not recommended for acute, subacute, chronic low back pain, and radicular pain syndrome based on evidence that the treatment is ineffective or that harms and cost exceed benefits to the patient (Evidence Rating B: moderate evidence).

Sacroiliac joint corticosteroid injection is recommended as an option for patients with specified known cause of sacroiliitis (Evidence Rating C: limited evidence).

The use of epidural glucocorticosteroid injection is not recommended for acute, subacute, or chronic low back pain in the absence of radicular signs and symptoms (Evidence Rating C: limited evidence).

Sacroiliac joint corticosteroid injection is not recommended for acute low back pain, including pain thought to be sacroiliac joint related, based on high costs or potential harm to the patient (Evidence Rating I: insufficient evidence).

The use of intradiscal steroids is not recommended for acute low back pain (Evidence Rating I: insufficient evidence), subacute, or chronic low back pain (Evidence Rating B: moderate evidence).

**American College of Physicians and the American Pain Society (2007)<sup>42</sup>:**

*Diagnosis and treatment of low back pain: a joint clinical practice guideline*

Epidural steroid injection is an option for patients with prolapsed lumbar disc with persistent radicular symptoms who have not responded to noninvasive therapy. No specific recommendation is given for this or any other injection therapy of interest.

**North American Spine Society (2007):**

*Diagnosis and treatment of degenerative lumbar spinal stenosis (NGC:005896)*

The NASS recommends nonfluoroscopically-guided interlaminar epidural steroid injection as a treatment option for short-term symptom relief in patients with neurogenic claudication or radiculopathy. A single radiographically-guided transforaminal injection may also provide short-term symptom relief for patients with radiculopathy (Grade B: fair evidence).

A multiple injection regimen of radiographically-guided transforaminal epidural steroid injection or caudal injections may provide long-term symptom relief in patients with radiculopathy or neurogenic intermittent claudication, but evidence supporting this recommendation is of poor quality.

**EuroCOST: European evidence-based guideline COST B13 Working Group on Guidelines for Chronic Low Back Pain (2006)<sup>3</sup>:**

*European guidelines for the management of chronic nonspecific low back pain*

Epidural steroid injection, facet joint injection, and facet nerve blocks are not recommended based on a lack of evidence or conflicting evidence.

Intradiscal injections are not recommended for the treatment chronic nonspecific low back pain based on evidence they are not effective (level B: moderate evidence).

**American Association of Neurological Surgeons; Congress of Neurological Surgeons (2005):**

*Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 13: injection therapies, low-back pain, and lumbar fusion (NGC:005374)*

Lumbar epidural injections and facet injections are recommended as treatment options for temporary, symptomatic relief in some patients with chronic low back pain, but epidural injections are not recommended for long-term relief of pain, based on Class III evidence (unclear clinical certainty). Facet injections are not recommended as long-term treatment for low back pain based on Class I evidence (high clinical certainty).

## ***2.9. Previous Systematic Reviews/Technology Assessments***

We found only one HTA on this subject<sup>31</sup>. One evidence report<sup>40</sup> with a subsequent systematic review (SR) publication<sup>39</sup> and a Clinical Guideline for the American Pain Society<sup>41</sup> were identified. The systematic review was conducted by AHRQ's Oregon Evidence-based Practice Center. We used this SR as the evidence base for data through July 2008. It is not summarized in this section; rather, summaries of the SR are included throughout this HTA. In addition, the Chou et al. SR is critically appraised in section 3.2.2.

We summarize in this section systematic reviews on the cervical spine published from 2007, and on the lumbar spine from 2008. Five cervical SRs are summarized<sup>18, 34, 56, 98, 160</sup>: three reports on epidural injections<sup>18, 34, 160</sup> and three reports on facet joint injections<sup>34, 56, 98</sup>. In the lumbosacral spine, thirteen SRs are summarized<sup>30, 46, 48, 75, 76, 80, 107, 113, 158, 165, 170, 175, 190</sup>: eleven evaluate epidural injections<sup>30, 46, 75, 76, 80, 107, 113, 158, 165, 170, 190</sup>, six evaluate facet joint or medial branch nerve injections<sup>48, 76, 80, 107, 113, 190</sup>, three evaluate injections of the sacroiliac joint<sup>107, 113, 175</sup> and one assesses intradiscal injections<sup>107</sup>. Table 2 summarizes these previous systematic reviews.

**Table 2: Overview of previous systematic reviews of spinal injections**

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Manchikanti (2009) <sup>113</sup>  <i>Comprehensive review of therapeutic interventions in managing chronic spinal pain</i>	NR	Lumbar spine  Caudal epidural steroid injection  Interlaminar epidural steroid injection  Transforaminal epidural steroid injection  Facet joint intraarticular injections  Medial branch blocks  Sacroiliac joint injections	<u>Epidural injections</u> 4 SR Caudal: 10 RCTs (% f/u NR); N=532; compared steroid injection to multiple therapies 4 observational studies (% f/u NR); N=196  Interlaminar: 8 RCTs (% f/u NR); N=659; compared epidural injection to multiple therapies 1 observational study (% f/u NR); N=84  Transforaminal: 4 RCTs (% f/u NR); N=502; compared epidural injections to multiple therapies  <u>Intraarticular facet joint injections</u> 4 SR  <u>Medial branch blocks</u> 4 RCTs (% f/u NR); N=244; compared steroid medial branch blocks with or without anesthetic to anesthetic (3) or anesthetic plus Sarapin (1)  2 observational studies (% f/u NR); N=155  4 SR	Yes	none	<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors conclude the recommendation for the use of caudal epidural steroids to manage lumbar spinal pain with disc herniation and radiculitis or pain without disc herniation or radiculitis is 1A or 1B/strong; for interlaminar epidurals in the same patient group it is 1C/strong ††</li> <li>The recommendation for caudal epidural steroids to manage post surgery syndrome and spinal stenosis is 1B or 1C/strong; for interlaminar epidurals in the same patient group it is 2C/very weak</li> <li>The recommendation for cervical interlaminar epidurals is 1C/strong</li> <li>The recommendation for lumbar transforaminal epidurals is 1C/strong</li> <li>There is a lack of evidence for the use of intraarticular facet joint injections, and therefore do not recommend their use.</li> <li>The recommendation for the use of medial branch blocks is strong (1B or 1C) for short and long-term pain relief from chronic facet joint pain. ††</li> <li>No evidence was found for sacroiliac joint injections.</li> </ul> <b>Safety</b> <ul style="list-style-type: none"> <li>Complications of epidural steroid injections and medial branch blocks are classified as being related to needle placement and drug administration. Serious complications include neural and vascular trauma, infection and intravascular injection.</li> </ul> <b>Economic</b> <ul style="list-style-type: none"> <li>Medial branch blocks were found to have a cost of \$3,461 for one year of improvement of QOL.</li> <li>One study found the cost effectiveness of fluoroscopically-directed caudal epidural steroid was \$3,365, transforaminal steroid was \$2,927, and interlaminar steroid was \$6,024</li> </ul>

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Levin (2009) <sup>107</sup>  <i>Prospective, double-blind, randomized placebo-controlled trials in interventional spine: what the highest quality literature tells us</i>	Though 12/2007	Lumbar epidural steroid injection  Facet joint injection/medial branch blocks  Sacroiliac joint injection  Intradiscal steroid injection	<u>Epidural steroid injection</u> 5 RCTs (% f/u NR); N=372; compared fluoroscopically-guided injection to anesthetic, saline, or other therapies  <u>Facet joint injection/medial branch blocks</u> 4 RCTs (% f/u NR); N=351; compared facet joint injection or medial branch block to saline, anesthetic and/or Sarapin  <u>Sacroiliac joint injection</u> 1 RCT (% f/u NR): N=10; compared steroid injection vs. saline  <u>Intradiscal steroid injection</u> 2 RCTs (% f/u NR); N=145; compared steroid injection to anesthetic or saline	No	Authors included treatments “similar” those of interest in analysis (e.g. selective nerve root injection as epidural injection)	<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors conclude that fluoroscopically-guided lumbosacral transforaminal epidural steroid injections are more effective than placebo at preventing surgery, and are effective at relieving pain in the short-term for patients with acute/subacute radicular pain.</li> <li>Authors conclude cervical facet joint injections are not more effective than placebo at treating patients with whiplash or chronic cervical or lumbar facet joint pain.</li> <li>Based on one RCT, authors conclude sacroiliac joint injections are more effective than placebo at one month for patients with spondyloarthropathy and low back pain.</li> <li>Based on 2 RCTs, authors conclude intradiscal steroid injections are not more effective than placebo in the short term or long term for select patients with radicular or discogenic pain.</li> </ul> <b>Safety:</b> NR  <b>Economic:</b> NR
Hall (2008) <sup>76</sup>  <i>Low back pain (chronic)</i>	Through 5/2007	Lumbar epidural steroid injection  Facet joint injection	<u>Epidural steroid injection</u> 1 SR No RCTs found by authors or in SR found to be relevant  <u>Facet joint injection</u> 2 RCTs (% f/u NR) N=161; compared facet joint injection to placebo 1 SR	No	Old SR (search through 1996)	<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors found no evidence to support the use of epidural steroid injections or facet joint injections in patients with chronic back pain without sciatica</li> </ul> <b>Safety</b> <ul style="list-style-type: none"> <li>One RCT reported transient pain at the injection site. Another noted potential serious side effects including infection, hemorrhage and neurological damage</li> </ul> <b>Economic:</b> NR

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Hall (2008) <sup>75</sup>  <i>Low back pain (acute)</i>	Through 5/2007	Lumbar epidural steroid	<u>Epidural steroid injection</u> 1 SR No RCTs found by authors or in SR found to be relevant	No	Based on old SR (search through 1998)	<b>Efficacy</b> <ul style="list-style-type: none"><li>Authors conclude that there is no evidence available supporting the use of epidural steroid injections to treat patients with acute low back pain</li></ul> <b>Safety</b> <ul style="list-style-type: none"><li>Authors note that epidural steroid injections have been associated with serious side effects (specific complications not described)</li></ul> <b>Economic:</b> NR
Buenaventura (2009) <sup>30</sup>  <i>Systematic review of therapeutic lumbar transforaminal epidural steroid injections</i>	Through 11/2008	Lumbar transforaminal epidural steroid injection	<u>Lumbar transforaminal epidural steroid injection</u> 4 RCTS (% f/u NR); N=502; all compared epidural steroid to: saline injection (1), bupivocaine injection (1), trigger point injection (1), another steroid injection location (1)	Yes	Level of evidence is II-1 for short-term relief and II-2 for long-term relief (USPSTF) **	<b>Efficacy</b> <ul style="list-style-type: none"><li>All 4 RCTs had evidence of short-term (within 6 months) symptom relief and 2 had evidence of long-term (over 6 months) symptom relief.</li><li>Recommendation classified as 1C/strong with benefits outweighing risks of treatment based on limited data. ††</li></ul> <b>Safety</b> <ul style="list-style-type: none"><li>Complications data not reported for RCTs, but authors cite neural trauma, vascular trauma, intravascular injection, infection, headaches and increased back pain as potential complications based on observational data.</li></ul> <b>Economic</b> <ul style="list-style-type: none"><li>One RCT found lower costs of drugs and therapy at 4-week follow-up, but not at other times.</li><li>One RCT found steroid injection prevented surgery for contained herniations with a cost savings of \$12,666 per patient.</li></ul>

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Staal, the Cochrane Collaboration (2008) <sup>190</sup>  <i>Injection therapy for subacute and chronic low-back pain</i>	1/1999 to 3/2007	Lumbar epidural steroid injection  Facet joint injection	<u>Epidural corticosteroid</u> 5 RCTs (% f/u NR); N=339; two compared epidural steroid to placebo injection, three compared epidural steroid to other therapies (NSAIDs, morphine, intrathecal benzodiazepine)  <u>Facet joint injection</u> 7 RCTs (% f/u NR); N=590; two compared steroid injection to placebo, four compared steroid injection to other therapies (anesthetic, home exercise, nerve blocks, sodium hyaluronate), one compared anesthetic injection to placebo	Yes	Updated review from Nelemans (2000)	<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors conclude there is insufficient evidence to support the use of injection therapy for subacute and chronic low back pain.</li> </ul> <u>Epidural corticosteroid</u> <ul style="list-style-type: none"> <li>Two RCTs that compared epidural corticosteroid to placebo injection found no significant results for pain relief or other outcomes; three RCTs that compared epidural corticosteroid to other treatments found no significant results for pain relief or other outcomes.</li> </ul> <u>Facet joint injection</u> <ul style="list-style-type: none"> <li>Most RCTs found no difference in short or long term outcomes for pain or functional status; one RCT found facet joint injection with lidocaine reduced pain immediately after procedure compared to saline injection; another found improvement at 6 months in patients given steroid injection vs. placebo.</li> </ul> <b>Safety</b> <u>Epidural corticosteroid</u> <ul style="list-style-type: none"> <li>One RCT found 2 patients with the theca penetrated by the needle during injection. No other serious complications noted.</li> <li>One RCT found 21% of patients reported transient headache or dizziness immediately after the procedure.</li> </ul> <u>Facet joint injection</u> <ul style="list-style-type: none"> <li>No serious complications were noted.</li> </ul> <b>Economic:</b> NR

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Datta (2009) <sup>48</sup>  <i>Systematic assessment of diagnostic accuracy and therapeutic utility of lumbar facet joint interventions</i>	Through 12/2008	Lumbar facet joint nerve blocks	<u>Lumbar facet joint nerve blocks</u> 2 RCTs (% f/u NR); N=320; one compared steroid plus anesthetic to local anesthetic, the second compared steroid plus anesthetic and Serapin to anesthetic and Serapin	Yes	No comparison with placebo  Level of evidence II-1 or II-2 (USPSTF)**	<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors conclude the recommendation is strong (1B or 1C) for the use of facet joint nerve blocks to provide short and long-term pain relief from chronic lumbar facet joint pain. ††</li> <li>One RCT found significant pain relief in 82% of patients and significant improvement in functional status in 78% of patients, but differences were not significant between patients treated with steroid plus anesthetic vs. anesthetic alone.</li> <li>Another RCT found similar positive results, but also did not find significant differences between patients treated with steroid plus anesthetic and Serapin vs. anesthetic and Serapin alone.</li> </ul> <b>Safety:</b> NR  <b>Economic:</b> NR

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Conn (2009) <sup>46</sup>  <i>Systematic review of caudal epidural injections in the management of chronic low back pain</i>	Through 11/2008	Caudal epidural injections	<p><u>Disc herniation and radiculitis</u> 6 RCTs (% f/u NR); N=328; compared caudal epidural steroid to anesthetic injection, saline injection, targeted steroid, intramuscular injection</p> <p><u>Post surgery syndrome and Spinal Stenosis</u> 3 RCTs (% f/u NR); N=169; one compared caudal epidural injection of anesthetic vs. anesthetic plus Celestone, another compared forceful epidural steroid injection vs. epidural steroid, a third compared epidural steroid vs. intramuscular placebo or steroid</p> <p>2 observational studies (% f/u NR); N=64; spinal stenosis only</p> <p><u>Discogenic pain</u> 1 RCT (% f/u NR); N=64; compared steroid plus anesthetic injection vs. anesthetic only</p> <p>2 observational studies (%f/u NR); N=132</p>	Yes	Level of evidence is I for disc herniation and radiculitis, II-1 or II-2 for post-surgery syndrome and spinal stenosis, and level I for discogenic pain**	<p><b>Efficacy</b> <u>Disc herniation and radiculitis</u></p> <ul style="list-style-type: none"> <li>Five of 6 RCTs found positive short-term pain relief results and 3/6 found positive long-term results.</li> <li>The two highest-quality RCTs with caudal epidural injection performed under fluoroscopy found improvements in patient pain scores, but results were not significant between treatment groups.</li> </ul> <p><u>Post surgery syndrome</u></p> <ul style="list-style-type: none"> <li>All 3 RCTs found positive short-term and long-term relief from pain symptoms.</li> </ul> <p><u>Spinal stenosis</u></p> <ul style="list-style-type: none"> <li>The RCT and both observational studies found evidence of positive short-term relief and 2/3 found positive long-term relief.</li> </ul> <p><u>Discogenic pain</u></p> <ul style="list-style-type: none"> <li>The RCT and both observational studies found evidence of positive short-term relief and 2/3 found positive long-term relief.</li> </ul> <p><b>Safety</b></p> <ul style="list-style-type: none"> <li>Complications across studies included soreness at injection site (18%), intravascular placement (14%), increased pain (5%), insomnia (4.7%), muscle spasms (4%), headaches (3-3.5%), minor bleeding (2%), nausea, dizziness and fever (all 1%).</li> </ul> <p><b>Economic</b></p> <ul style="list-style-type: none"> <li>One study found the cost of fluoroscopy-directed caudal epidural steroids was \$3,635; transforaminal steroids was \$2,927 per year; and the cost of interlaminar steroids was \$6,024.</li> <li>Another study found the cost of a one-year improvement for quality of life was \$2,550 in patients treated with caudal epidural anesthetic and/or steroid injection.</li> </ul>

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Henschke (2010) <sup>80</sup>  <i>Injection therapy and denervation procedures for chronic low-back pain: a systematic review</i>	Through 11/2009	Lumbar epidural injection  Facet joint injection	<u>Epidural injection</u> 3 RCTs (% f/u NR); N=128; compared steroid and/or anesthetic to other therapies (no placebo comparisons)  <u>Facet joint injection</u> 7 RCTs (% f/u NR); N=619; compared steroid and/or anesthetic to placebo or other therapies	Yes		<p><b>Efficacy</b></p> <ul style="list-style-type: none"> <li>Authors conclude there is low to very low quality evidence for injection therapy to treat chronic low back pain.</li> </ul> <p><u>Epidural injection</u></p> <ul style="list-style-type: none"> <li>Two RCTs that compared epidural steroid injection with other treatments found no significant differences in outcomes between treatment groups.</li> <li>One RCT that compared epidural anesthetic injection with other treatment found no significant differences in outcomes between groups</li> </ul> <p><u>Facet joint injection</u></p> <ul style="list-style-type: none"> <li>Two RCTs that compared steroid facet joint injection to placebo found no significant differences between treatment groups for pain at short-term follow up, but one study found improvements at 6 months in the injection group.</li> <li>One out of 5 RCTs that compared steroid facet joint injection to other therapies found the injections provided significant pain relief at one month compared to facet nerve blocks; no other studies found differences in the short or long-term between treatments.</li> <li>One RCT that compared anesthetic facet joint injection to placebo found significant pain relief after treatment.</li> </ul> <p><b>Safety</b></p> <p><u>Epidural injection</u></p> <ul style="list-style-type: none"> <li>One RCT found 57% of steroid epidural patients reported headache and 14% reported nausea post-procedure</li> </ul> <p><u>Facet joint injection</u></p> <ul style="list-style-type: none"> <li>Two RCTs reported minor complications, including transient pain at injection site, headache and nausea.</li> </ul> <p><b>Economic:</b> NR</p>

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Roberts (2009) <sup>170</sup>  <i>Efficacy of lumbosacral transforaminal epidural steroid injections: a systematic review</i>	Through 5/2008	Lumbosacral transforaminal epidural steroid injection	<u>Lumbosacral transforaminal epidural steroid injection</u> 9 RCTs (% f/u NR); N=617; 1 compared transforaminal injection to placebo, 4 compared transforaminal injection to another treatment (anesthetic or trigger point injection), 4 compared transforaminal injection to interlaminar or caudal injection	Yes		<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors conclude there is good evidence that transforaminal steroid injection is superior to interlaminar and caudal steroid injection, and that it should be used as a surgery-sparing treatment in patients with radicular pain.</li> <li>Authors also conclude there is fair evidence that transforaminal steroid injection is superior to placebo to treat radicular symptoms and prevent disability.</li> <li>For patients with subacute or chronic radicular symptoms, authors conclude that transforaminal steroid injection is comparable to anesthetic or saline injection.</li> </ul> <b>Safety:</b> NR  <b>Economic:</b> NR
Rabinovitch (2009) <sup>165</sup>  <i>Influence of lumbar epidural injection volume on pain relief for radicular leg pain and/or low back pain</i>	Through 1/2009	Lumbar epidural steroid injection	<u>Lumbar epidural steroid injection</u> 1 CCT (% f/u ); N=48; compared epidural steroid with saline 14 RCTs (% f/u NR); N=838; compared epidural steroid or anesthetic with saline, anesthetic, or other treatment	Yes	Individual study outcomes not described	<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors conclude that the correlation between volume of injection and pain relief for immediate term (<math>\leq 6</math> weeks) was 0.8027; for short term (<math>&gt;6</math> weeks-3 months) it was 0.5019; for intermediate term (<math>&gt;3</math> months-1 year) it was 0.9470.</li> </ul> <b>Safety:</b> NR  <b>Economic:</b> NR

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Parr (2009) <sup>158</sup>  <i>Lumbar interlaminar epidural injections in managing chronic low back and lower extremity pain: a systematic review</i>	Through 11/2008	Lumbar interlaminar epidural steroid injection	<u>Lumbar interlaminar epidural steroid injection</u> 5 RCTs (% f/u NR): N=553; compared steroid injection with intramuscular injection, saline, or anesthetic  2 observational studies (% f/u NR); N=316	Yes	Level of evidence is II-2 for managing low back pain secondary to disc herniation and/or radiculitis  Level of evidence is III for spinal stenosis and low back pain without disc herniation and/or radiculitis (USPSTF)**	<b>Efficacy</b> <u>Disc herniation and radiculitis</u> <ul style="list-style-type: none"> <li>Two of 5 relevant RCTs had evidence of short-term improvement in pain relief for patients with disc herniation and radiculitis.</li> <li>Based on available evidence, authors conclude recommendation for short-term relief is 1C/strong, with benefits outweighing risks of treatment for patients. ††</li> </ul> <u>Spinal stenosis</u> <ul style="list-style-type: none"> <li>One of 3 relevant studies (2 RCTs, 1 observational) had evidence of short-term improvement in pain relief for patients with spinal stenosis.</li> <li>Based on available evidence, authors conclude recommendation is 2C/weak with other alternatives may be equally effective.</li> </ul> <u>Low back pain without disc herniation or radiculitis</u> <ul style="list-style-type: none"> <li>No RCTs addressed outcomes in patients with low back pain without disc herniation or radiculitis. One observational study found positive short-term improvement in pain, but negative results in the long-term.</li> <li>Based on available evidence, authors conclude recommendation is 2C/weak with other alternatives may be equally effective.</li> </ul> <b>Safety</b> <ul style="list-style-type: none"> <li>Complications are classified as being related to needle placement or drug administration. No complications from included studies are cited.</li> </ul> <b>Economic</b> <ul style="list-style-type: none"> <li>Authors conclude from evidence from two studies that interlaminar epidural steroid injection is not cost-effective.</li> </ul>

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Rupert (2009) <sup>175</sup>  <i>Evaluation of sacroiliac joint interventions: a systematic appraisal of the literature</i>	Through 2008	Intraarticular sacroiliac joint injection	All RCTs and observational studies excluded due to lack of valid diagnosis prior to intervention and other methodological problems	Yes		<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors conclude evidence is unavailable to evaluate therapeutic intraarticular sacroiliac joint injection.</li> </ul> <b>Safety:</b> NR  <b>Economic:</b> NR
Canadian Agency for Drugs and Technologies in Health (2007) <sup>31</sup>  <i>Facet joint injection as a diagnostic and therapeutic tool for spinal pain: areview of clinical and cost-effectiveness</i>	Through 8/2006	Facet joint injection	<u>Facet joint injection</u> 7 RCTs (% f/u NR); N=529; compared facet joint injection with nerve block, medial branch block, exercise, saline or anesthetic  9 case series (% f/u NR); N=929  2 SR  1 HTA (diagnostic injection only)  3 practice guidelines (ACR, ASIPP, ECRDG)	No	One SR cited has since been withdrawn (Nelemans 2000)  Authors evaluated both diagnostic and therapeutic injection; not clear which studies contained each approach	<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors conclude based on evidence from RCTs that facet joint injections with steroid or anesthetic are not superior to placebo for the treatment of chronic low back pain.</li> <li>Authors also conclude steroid facet joint injection is not superior to anesthetic injection for the treatment of neck pain secondary to motor vehicle accident.</li> <li>Additional well-designed RCTs with appropriate diagnostic procedures are needed to show the effectiveness of therapeutic facet joint injection.</li> </ul> <b>Safety:</b> <ul style="list-style-type: none"> <li>Among the 2 studies (both case series) that reported side effects, no serious complications were noted.</li> <li>One study found a 6.1% rate of intravascular uptake.</li> </ul> <b>Economic:</b> <ul style="list-style-type: none"> <li>Authors note that funding for facet joint injection is inconsistent across Canada and codes for other procedures are often used when billing for facet joint injection.</li> </ul>

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
<p>Institute for Clinical Systems Improvement (2004)<sup>90</sup></p> <p><i>Fluoroscopically guided transforaminal epidural steroid injections for lumbar radicular pain</i></p>	NR	Transforaminal epidural steroid	<p><u>Epidural steroid</u></p> <p>2 RCTs (100% f/u &amp; 99% f/u); N=216; compared transforaminal steroid injection to saline</p> <p>3 case series (% f/u NR); N=149</p> <p>1 SR</p>	Yes	<p>Both RCTs blinded participants and treating physicians</p> <p>Conclusions Grade III§</p>	<p><b>Efficacy</b></p> <ul style="list-style-type: none"> <li>One RCT found patients given steroid injections had lower rates of surgery at mean 23 months follow-up.</li> <li>The second RCT found patients given steroid injections reported less pain immediately after treatment, but not over long-term follow-up.</li> <li>Authors report that patients who have lumbar radicular pain at one or two levels may be good candidates for steroid injections to avoid surgery, but conclude that there is insufficient evidence to comment on the overall efficacy of epidural steroid injections.</li> </ul> <p><b>Safety:</b></p> <ul style="list-style-type: none"> <li>Authors conclude that transforaminal epidural steroid injections should always be performed under the guidance of fluoroscopy.</li> <li>One study found 4 complications requiring hospitalization or ER visit in a series of 5,334 patients treated with epidural injections (multiple approaches).</li> </ul> <p><b>Economic:</b></p> <ul style="list-style-type: none"> <li>The 2004 Medicare reimbursement rate for transforaminal steroid injection at a single lumbar or sacral level was \$357 with \$157 for each additional level. Fluoroscopy and facility fees are not included.</li> <li>One RCT found lower costs of therapy visits and medications in patients given steroid injections.</li> </ul>

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Peloso, the Cochrane Collaboration (2006) <sup>160</sup>  <i>Medicinal and injection therapies for mechanical neck disorders</i>	Through 3/2003	Cervical epidural steroid	<u>Cervical epidural steroid</u> 1 RCT (84% f/u); N=50; compared epidural methylprednisolone plus lidocaine vs. placebo	Yes		<b>Efficacy</b> <ul style="list-style-type: none"> <li>One RCT found statistically significant evidence of pain relief and return to work at one year for patients treated with epidural steroid compared with placebo</li> <li>Authors concluded there is limited evidence of benefit of epidural methylprednisolone in chronic mechanical neck disorder with radicular findings.</li> </ul> <b>Safety:</b> NR  <b>Economic:</b> NR
Carragee (2008) <sup>34</sup>  <i>Treatment of neck pain: injections and surgical interventions: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders</i>	Through 2006	Cervical epidural steroid  Cervical facet injection	<u>Cervical epidural steroid</u> 1 RCT (% f/u NR); N=NR/42; one compared epidural vs. paraspinal injection  1 retrospective survey of complications (% f/u NR); N=NR  <u>Cervical facet joint injection</u> 1 RCT (% f/u NR); N=42; compared corticosteroid intra-articular injection plus bupivacaine vs. bupivacaine only  2 prospective surveys of complications (% f/u NR); N=NR	Yes		<b>Efficacy</b> <u>Epidural corticosteroid</u> <ul style="list-style-type: none"> <li>Concluded there is evidence of short-term symptomatic improvement in radicular symptoms with a short course (&lt;4) of injections.</li> </ul> <u>Cervical facet injection</u> <ul style="list-style-type: none"> <li>Concluded there is no evidence to support treatment with cervical facet injection.</li> </ul> <b>Safety</b> <u>Epidural corticosteroid</u> <ul style="list-style-type: none"> <li>One retrospective survey found 7% of patients reported increased pain, 5% reported headache and there was one puncture of the dura mater.</li> </ul> <u>Other injections</u> <ul style="list-style-type: none"> <li>A prospective survey of selective nerve root blocks found subjects reported pain at the injection site (23%), increased radicular pain (18%), lightheadedness (14%), increased spine pain, headache, and nausea (3-10%).</li> <li>A second prospective survey of extraforaminal cervical root injections found no serious neurological events.</li> </ul> <b>Economic:</b> NR

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Benyamin (2009) <sup>18</sup>  <i>Systematic review of the effectiveness of cervical epidurals in the management of chronic neck pain</i>	Through 11/2008	Cervical interlaminar epidural injection	<u>Cervical interlaminar epidural injection</u> 3 RCTs (% f/u NR); N=209; one compared steroid vs. steroid plus morphine, another compared steroid plus lidocaine in epidural vs. posterior neck muscle injection, the third compared epidural steroid administered in single block injections vs. continuous epidural  2 prospective uncontrolled (% f/u NR); N=87  3 retrospective (% f/u NR); N=186	Yes	Level of evidence is II-1 (USPSTF)**  Observational studies not included in evidence synthesis	<b>Efficacy</b> <ul style="list-style-type: none"> <li>All 3 RCTs had evidence of short-term (within 6 months) symptom relief and 2 had evidence of long-term (6 months-1 year) symptom relief.</li> <li>Recommendation classified as 1C/strong with benefits outweighing risks of treatment based on limited data. ††</li> <li>All observational studies suggested improvement in pain relief and 2 suggested positive results in returning to normal activities in daily living.</li> </ul> <b>Safety</b> <ul style="list-style-type: none"> <li>Complications data not reported for RCTs, but authors cite subarachnoid entry, subdural entry, spinal cord trauma, infection, hematoma formation, abscess formation, intracranial air injection, epidural lipomatosis, nerve damage, headache, brain damage, increased intracranial pressure, intravascular injection, vascular injury, cerebrovascular or pulmonary embolus, and death as the most common serious complications based on observational data.</li> </ul> <b>Economic:</b> NR

Assessment (year)	Search dates	Treatments evaluated	Evidence base available*†	Critical appraisal‡	Comments	Primary Conclusions
Falco (2009) <sup>§</sup>  <i>Systematic review of diagnostic utility and therapeutic effectiveness of cervical facet joint interventions</i>	Through 12/2008	Cervical medial branch block	<u>Cervical medial branch block</u> 1 RCT (100% f/u); N=120; compared cervical medial branch blocks with steroid plus bupivacaine vs. bupivacaine  1 observational study (% f/u NR); N=100	Yes	No comparison with placebo  Level of evidence is II-1 (USPSTF)**	<b>Efficacy</b> <ul style="list-style-type: none"> <li>Authors conclude the recommendation is strong (1B or 1C) for the use of facet joint medial branch blocks to provide short and long-term pain relief from chronic cervical facet joint neck pain. ††</li> <li>Both the RCT and the observational study found positive results for pain status from cervical medial branch blocks at short-term (within 6 months) and long-term (over 6 months) follow-up, but significant differences were not found between patients treated with steroid plus bupivacaine versus bupivacaine alone.</li> </ul> <b>Safety:</b> NR  <b>Economic:</b> NR

ACR: American College of Radiology

ASIPP: American Society of International Pain Physicians

ECRDG: European Commission Research Directorate General

f/u: follow up

NR: not reported

USPSTF: United States Preventive Services Task Force

\* Percent follow-ups were not given for all studies.

† N reflects numbers before loss to follow-up.

‡ Critical appraisal refers to formal evaluation of individual study quality using criteria such as the Jadad or GRADE methods of scoring and the determination of overall strength of evidence.

§ From conclusion grading worksheet completed by committee members. Grades range from I (evidence from strong studies with clinically important results) to III (evidence from strong studies, but with significant uncertainty attached to the conclusion due to inconsistent results across studies or flaws in study design).

\*\* The five levels of evidence were classified as level I (the highest level of evidence), II, or III (the lowest level of evidence) with three subcategories within level II based on the quality of evidence developed by the USPSTF.

†† Grade of recommendation based on Guyatt G et al. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. Chest 2006; 129:174-181. Grades range from 1A/strong recommendation with high quality evidence where benefits clearly outweigh the risks of treatment, to 2C/weak recommendation with low-quality or very low-quality evidence where there is Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced.

## 2.10. Medicare and Representative Private Insurer Coverage Policies

Coverage policies are consistent for the coverage of epidural steroid injection in select patients, although criteria for patient selection vary across plans. Documented success with diagnostic injections is frequently required to proceed to therapeutic injection. Coverage is not consistent for facet joint injections, sacroiliac joint injections, and intradiscal injections. When covered, injections are subject to spacing requirements between procedures, yearly and/or lifetime maximums.

### National policy decisions:

- Medicare
  - No national coverage decisions were found for any spinal injections.

- Aetna (2010)

Aetna will cover the following procedures as specified, but only one procedure will be covered at a time:

- Epidural injections: Aetna will cover epidural injections of corticosteroid preparations with or without anesthetic agents in the outpatient setting to relieve back or neck pain when **all** of the following conditions are met:
  - Intraspinal tumor or other space-occupying lesion, or non-spinal origin for pain, has been ruled out as the cause of pain;
  - Two or more weeks of treatment with conservative measures (e.g. rest, systemic analgesics and/or physical therapy) have not improved pain;
  - Epidural injections beyond the first set of three injections are provided as part of a comprehensive pain management program, which includes physical therapy, patient education, psychosocial support, and oral medications, where appropriate.

Repeat epidural injections more frequently than every 7 days are not covered. If a patient does not show improvement after up to three injections, additional injections will not be covered. Once a therapeutic effect is achieved, it is rarely medically necessary to repeat epidural injections more frequently than once every two months. In selected cases where more definitive therapies (e.g., surgery) cannot be tolerated or provided, additional epidural injections may be considered medically necessary. Repeat injections extending beyond 12 months may be reviewed for continued medical necessity.

Epidural injections are considered experimental and investigational for all other indications

- Selective nerve root blocks/selective transforaminal epidural injection: Aetna will cover selective nerve root blocks for patients with radiculopathy when other non-invasive measures (e.g. physical therapy, non-narcotic analgesics) have failed or become intolerant and **any one** of the following conditions is met:
  - Radicular pain that is due to post-surgical or post-traumatic scarring;
  - Radicular pain when surgically correctable lesion cannot be identified;
  - Radicular pain in persons with surgically correctable lesions but who are not surgical candidates.

Selective nerve root blocks should be administered as part of a comprehensive pain management program. Administration of more than three injections over six months is subject to review.

Selective nerve root blocks are considered experimental and investigational for all other indications.

- Facet joint injections: Aetna only considers diagnostic facet joint injections to be medically necessary. Therapeutic injections are classified as experimental and investigational as treatment for back and neck pain and for all other indications. Therapeutic facet joint injections are found to have no proven value.
- Sacroiliac joint injections: Aetna will cover sacroiliac joint injections when they are used to relieve pain associated with lower lumbosacral disturbances in patients, provided the patient meets **both** of the following conditions:
  - The patient has back pain for more than three months;
  - The injections are provided as part of a comprehensive pain management program, including physical therapy, patient education, psychosocial support, and oral medication where appropriate.

Aetna will cover up to two sacroiliac injections for diagnosis and treatment; additional injections are not covered if the patient experiences no symptom relief or functional improvement from two injections. It is not considered medically necessary to repeat these injections more frequently than once every 7 days. Once the diagnosis is established, it is rarely medically necessary to repeat sacroiliac injections more frequently than once every two months. Repeat injections extending beyond 12 months may be reviewed for continued medical necessity.

Sacroiliac joint injections are considered experimental and investigational for all other indications.

- CIGNA (2010)

Cigna will cover the following procedures as specified below. Ultrasound guidance for injections is considered experimental, investigational, or unproven and is not covered.

- Epidural steroid injection/selective nerve root block: CIGNA covers epidural steroid injection for acute or recurrent radicular pain when a trend toward improvement is not seen after at least three weeks of conservative treatment (e.g. pharmacological therapy, physical therapy, exercise).

CIGNA will cover up to two additional injections if patients experience at least three weeks of temporary, partial relief of symptoms following the initial injection, but radicular pain has worsened.

Long-term, repeated, or maintenance injection is not covered. Epidural steroid injection for acute, subacute, or chronic back pain is considered experimental, investigational, or unproven.

- Facet joint injection: CIGNA will only cover diagnostic facet joint injection. Therapeutic facet joint injection is not covered because it is considered experimental, investigational, or unproven.

- Sacroiliac joint injection: CIGNA will cover sacroiliac joint injection for the treatment of back pain associated with localized sacroiliac joint confirmed on imaging studies.
- Intradiscal steroid injection: CIGNA does not cover intradiscal steroid injection because it is considered experimental, investigational, or unproven.

- Humana (2010)

Humana will cover the following procedures as specified below. Ultrasound guidance for injections is considered experimental, investigational, or unproven and is not covered.

- Epidural steroid injection: Humana may cover therapeutic epidural steroid injection when **all** of the following conditions are met by the patient:
  - Failure to improve after six weeks of conservative therapy, including but not limited to, rest, systemic medications, and/or physical therapy;
  - Pain is radicular;
  - Diagnostic epidural steroid injection (two injections) is successful
  - Injections must be at least two months apart, provided the patient has at least 50% relief in pain and/or symptoms for six weeks;
  - A total of four therapeutic injections per region (cervical, thoracic, lumbar) may be given per rolling calendar year, provided the patient has responded to treatment for at least six weeks and pain has returned or function has declined.

Patients may also be eligible for epidural steroid injection if pain has been unresponsive to conservative measures and is related to diagnoses of cancer, reflex sympathetic dystrophy, lumbar spinal stenosis, or herpes zoster/post-herpetic neuralgia (total of six injections per rolling calendar year covered).

- Facet joint injections/medial branch blocks: Humana may cover cervical, thoracic, and lumbar therapeutic facet joint injections or medial branch blocks for neck or back pain when facet joint syndrome is suspected when **all** of the following conditions are met by the patient:
  - Absence of radiculopathy;
  - Pain that is aggravated by extension, rotation or lateral bending of the spine, and is not typically associated with neurological deficits
  - Diagnosis of pain was at least three months ago and has been unresponsive to conservative treatment (e.g. rest, medication, physical therapy);
  - No more than three levels of facet joint injections per side, per region may be injected per session;
  - Diagnostic injection (two series of injections) is successful
  - Injections must be at least two months apart, provided the patient has at least 50% relief in pain and/or symptoms for six weeks;
  - A total of four therapeutic injections per region (cervical, thoracic, lumbar) may be given per rolling calendar year, provided the patient has responded to treatment for at least six weeks and pain has returned or function has declined.
- Sacroiliac joint injection: Humana may cover sacroiliac joint injections if the patient has met **all** of the following conditions:
  - Chronic low back pain with symptoms for at least six weeks;

- Pain has been unresponsive to conservative treatment (e.g. rest, medication, physical therapy);
- Diagnostic injection is successful with an 80% reduction in pain and/or symptoms;
- Injections must be at least two months apart, provided the patient has at least 50% relief in pain and/or symptoms for six weeks;
- A total of four therapeutic injections per joint may be given per rolling calendar year, provided the patient has responded to treatment for at least six weeks and pain has returned or function has declined.

- UnitedHealthcare (2010)

UnitedHealthcare will cover the following procedures as specified below.

- Epidural steroid injection: UnitedHealthcare will cover epidural steroid injection for patients with acute and sub-acute sciatica or radicular pain caused by spinal stenosis, disc herniation, or degenerative changes in the vertebrae. They are approved for short-term use provided the following conditions are met by the patient:
  - The pain is associated with symptoms of nerve root irritation and/or low back pain due to disc extrusions and/or contained herniations;
  - The pain has been unresponsive to conservative treatment (e.g. medications, physical therapy, exercise).
- Facet joint injection: UnitedHealthcare will only cover diagnostic facet joint injection. Therapeutic facet joint injection is considered unproven due to conflicting clinical evidence for facet joint syndrome and a lack of evidence for the effectiveness of facet joint injections over placebo at reducing chronic spinal pain.

### Local policy decisions:

- CMS Local Coverage Decisions (2010)

A combination of epidural injections, facet joint injections, bilateral sacroiliac joint injections, or lumbar sympathetic blocks on one day is not considered medically necessary.

- Epidural injection (most states, including Washington, Idaho, and Oregon): Epidural injections, both interlaminar/translaminar and transforaminal, should be used only in the presence of radiculopathy. A multi-disciplinary or collaborative comprehensive evaluation is recommended before initiating treatment with epidural steroid injection. Epidural injections are indicated for the following patients:
  - Radicular pain resistant to more conservative measures or when surgery is contraindicated
  - Post-decompressive radiculitis or post-surgical scarring
  - Monoradicular pain, confirmed by diagnostic block in which a surgically correctible lesion cannot be identified
  - Treatment of acute herpes zoster or post herpetic neuralgia

Patients must meet the following conditions for epidural injection to be considered medically necessary:

- Epidural injections should not exceed a series of three per spinal region in a six-month period. They may be performed at intervals of one week or greater.
- With each subsequent injection the medical record should clearly document the interval effect(s) from the prior injection.

- If two injections have not provided improvement in pain or functional status, a third injection should not be given unless a compelling technical reason is present.
  - Fluoroscopic guidance must be used for single nerve root/transforaminal injections to ensure proper needle placement.
  - Injections for chronic pain that are not performed under imaging (fluoroscopy or CT) guidance are not considered medically necessary.
- Facet joint injection (most states, including Washington, Idaho, and Oregon): Facet joint injections are considered medically necessary for the treatment of chronic pain that has failed to respond to more conservative treatment. Radiculopathy should be ruled out before proceeding with facet joint injection. Providing more than three levels of facet joint blocks on the same day is not considered medically necessary.
  - No more than four injections per region per patient should be administered in a one year period.
  - Facet joint injections not performed under the guidance of fluoroscopy or CT imaging are not considered medically necessary.
- BCBS Regence Group (Idaho, Oregon, Utah, and most of Washington) (2009)
  - Facet joint injection: Therapeutic facet joint injection may be covered when performed under fluoroscopy for the management of chronic neck or back pain (pain lasting at least three months despite conservative treatment such as physical therapy and non-steroidal anti-inflammatory medication). Facet joint injections for the treatment of acute back or neck pain are not considered medically necessary. Patients must meet the following criteria for injections to be considered medically necessary:
    - One injection per level per side every two months or longer provided the patient has achieved at least 50% pain relief in six weeks. The medical record must clearly document responsiveness to prior injections indicating improvement in physical and functional status;
    - Injections are limited to a maximum of six per year;
    - A maximum of 16 injections in a lifetime is rarely considered medically necessary. Exceptions to the lifetime limit include:
      - Pathology involving both cervical and lumbar spine;
      - Bilateral facet joint injections;
      - Recurrence of symptoms at least two years after previous successful facet joint injection treatments.

Injection of viscosupplementation agent (Hyaluronic acid) is considered investigational.

**Table 3. Overview of payer technology assessments and policies for spinal injections**

Payer (Year)	Lit search dates	Evidence base available	Policy	Rationale / comments
<b>National policies</b>				
<p>Aetna Clinical Policy Bulletin: Back Pain – Invasive Procedures (0016) (2010)</p> <p>Clinical Policy Bulletin: Selective Nerve Root Blocks (0722) (2010)</p>	NR	<p><u>Epidural injection:</u> 1 practice guideline (AAN)</p> <p><u>Selective nerve root blocks:</u> 1 RCT 5 observational studies 1 case series 2 SR 1 technology assessment (ICSI)</p> <p><u>Facet joint injection:</u> 2 RCTs 1 SR 4 practice guidelines (APS, AANS, ACOEM, CADTG)</p> <p><u>Sacroiliac joint injection:</u> NR</p>	<p>Aetna will cover the following procedures as specified, but only one procedure will be covered at a time:</p> <p><u>Epidural injection:</u> Aetna will cover epidural injections of corticosteroid preparations with or without anesthetic agents in the outpatient setting to relieve back or neck pain when all of the following conditions are met:</p> <ul style="list-style-type: none"> <li>• Intraspinous tumor or other space-occupying lesion, or non-spinal origin for pain, has been ruled out as the cause of pain;</li> <li>• Two or more weeks of treatment with conservative measures (e.g. rest, systemic analgesics and/or physical therapy) have not improved pain;</li> <li>• Epidural injections beyond the first set of three injections are provided as part of a comprehensive pain management program, which includes physical therapy, patient education, psychosocial support, and oral medications, where appropriate.</li> </ul> <p><u>Selective nerve root blocks/selective transforaminal epidural injection:</u> Aetna will cover selective nerve root blocks for patients with radiculopathy when other non-invasive measures (e.g. physical therapy, non-narcotic analgesics) have failed or become intolerant and any one of the following conditions is met:</p> <ul style="list-style-type: none"> <li>• Radicular pain that is due to post-surgical or post-traumatic scarring;</li> <li>• Radicular pain when surgically correctable lesion cannot be identified;</li> <li>• Radicular pain in persons with surgically correctable lesions but who are not surgical candidates.</li> </ul> <p>Selective nerve root blocks should be administered as part of a comprehensive pain management program.</p> <p><u>Facet joint injection:</u> not covered</p> <p><u>Sacroiliac joint injections:</u> Aetna will cover sacroiliac joint injections when they are used to relieve pain associated with lower lumbosacral disturbances in patients, provided the patient meets both of the following conditions:</p> <ul style="list-style-type: none"> <li>• The patient has back pain for more than three months;</li> <li>• The injections are provided as part of a comprehensive pain management</li> </ul>	<p>CPT codes if conditions are met: 64479, 64480, 64483, 64484, 64490, 64491, 64492, 64493, 64494, 64495, 27096, 62310, 62311, 62318, 62319, 0228T, 0229T, 0230T, 0231T</p>

Payer (Year)	Lit search dates	Evidence base available	Policy	Rationale / comments
			program, including physical therapy, patient education, psychosocial support, and oral medication where appropriate.	
CIGNA Medical Coverage Policy: Minimally Invasive Treatment of Back Pain (0139) (2010)	NR	<p><u>Epidural injection:</u> 2 SR 3 practice guidelines (ASIPP, ACOEM, AANS)</p> <p><u>Facet joint injection:</u> 1 SR 3 practice guidelines (ASIPP, ACOEM, AANS)</p> <p><u>Sacroiliac joint injection:</u> 3 practice guidelines (ASIPP, ACEOM, APS)</p> <p><u>Intradiscal injection:</u> 1 practice guideline (ACOEM)</p>	<p>Ultrasound guidance for injections is not covered</p> <p><u>Epidural steroid injection/selective nerve root block:</u> CIGNA covers epidural steroid injection for acute or recurrent radicular pain when a trend toward improvement is not seen after at least three weeks of conservative treatment (e.g. pharmacological therapy, physical therapy, exercise).</p> <p><u>Facet joint injection:</u> not covered</p> <p><u>Sacroiliac joint injection:</u> CIGNA will cover sacroiliac joint injection for the treatment of back pain associated with localized sacroiliac joint confirmed on imaging studies.</p> <p><u>Intradiscal steroid injection:</u> not covered</p>	CPT codes if conditions met: 27096, 62310, 62311, 64479, 64480, 64483, 64484, 64490, 64491, 64492, 64493, 64494, 64495, 77003
Humana Medical Coverage Policy: Injections for Pain Conditions (CPD-0486-004) (2010)	NR	NR	<p>Ultrasound guidance for injections is not covered</p> <p><u>Epidural steroid injection:</u> Humana may cover therapeutic epidural steroid injection when all of the following conditions are met by the patient:</p> <ul style="list-style-type: none"> <li>• Failure to improve after six weeks of conservative therapy, including but not limited to, rest, systemic medications, and/or physical therapy;</li> <li>• Pain is radicular;</li> <li>• Diagnostic epidural steroid injection (two injections) is successful</li> <li>• Injections must be at least two months apart, provided the patient has at least 50% relief in pain and/or symptoms for six weeks;</li> <li>• A total of four therapeutic injections per region (cervical, thoracic, lumbar) may be given per rolling calendar year, provided the patient has responded to treatment for at least six weeks and pain has returned.</li> </ul> <p>Patients may also be eligible if pain has been unresponsive to conservative measures and is related to diagnoses of cancer, reflex sympathetic dystrophy, lumbar spinal stenosis, or herpes zoster/post-herpetic neuralgia.</p> <p><u>Facet joint injections/medial branch</u></p>	CPT codes if conditions are met: 27096, 62310, 62311, 64470, 64472, 64475, 64476, 64479, 64480, 64483, 64484, 64490, 64491, 64492, 64493, 64494, 64495, 77003

Payer (Year)	Lit search dates	Evidence base available	Policy	Rationale / comments
			<p><u>blocks</u>: Humana may cover cervical, thoracic, and lumbar therapeutic facet joint injections or medial branch blocks for neck or back pain when facet joint syndrome is suspected when all of the following conditions are met by the patient:</p> <ul style="list-style-type: none"> <li>• Absence of radiculopathy;</li> <li>• Pain that is aggravated by extension, rotation or lateral bending of the spine, and is not typically associated with neurological deficits</li> <li>• Diagnosis of pain was at least three months ago and has been unresponsive to conservative treatment (e.g. rest, medication, physical therapy);</li> <li>• No more than three levels of facet joint injections per side, per region may be injected per session;</li> <li>• Diagnostic injection (two series of injections) is successful</li> <li>• Injections must be at least two months apart, provided the patient has at least 50% relief in pain and/or symptoms for six weeks;</li> <li>• A total of four therapeutic injections per region (cervical, thoracic, lumbar) may be given per rolling calendar year, provided the patient has responded to treatment for at least six weeks and pain has returned or function has declined.</li> </ul>	
UnitedHealthcare Medical Policy: Epidural Steroid and Facet Injections for Spinal Pain (2010T0004L) (2010)	NR	<p><u>Epidural steroid injection</u>: 7 RCTs 1 prospective cohort 1 SR 6 practice guidelines (ASA, AHRQ, AAN, ASIPP, AANS, NASS)</p> <p><u>Facet joint injection</u>: 6 RCTs 3 observational studies 2 SR 1 practice guideline (AHRQ)</p>	<p><u>Epidural steroid injection</u>: UnitedHealthcare will cover epidural steroid injection for patients with acute and sub-acute sciatica or radicular pain caused by spinal stenosis, disc herniation, or degenerative changes in the vertebrae. They are approved for short-term use provided the following conditions are met by the patient:</p> <ul style="list-style-type: none"> <li>• The pain is associated with symptoms of nerve root irritation and/or low back pain due to disc extrusions and/or contained herniations;</li> <li>• The pain has been unresponsive to conservative treatment (e.g. medications, physical therapy, exercise).</li> </ul> <p><u>Facet joint injection</u>: not covered</p>	CPT codes if conditions are met: 62311, 64483, 64484
<b>Local policies</b>				
Centers for Medicare and Medicaid Services Wisconsin	NR	<p><u>Epidural injection</u>: 3 SR 2 practice guidelines (AAN, NR)</p>	A combination of epidural injections, facet joint injections, bilateral sacroiliac joint injections, or lumbar sympathetic blocks on one day is not considered medically necessary.	CPT codes if conditions are met: 62281, 62282, 62310, 62311, 62318,

Payer (Year)	Lit search dates	Evidence base available	Policy	Rationale / comments
<p>Physicians Service Insurance Corporation</p> <p>LCD for Epidural and Transforaminal epidural injections (L30481) (2010)</p> <p>LCD for Paravertebral Facet Joint Block and Facet Joint Denervation (L30483) (2010)</p>		<p><u>Facet joint injection:</u> Other LCDs 1 practice guideline (NR)</p>	<p><u>Epidural injection:</u> Epidural injections, both interlaminar/translaminar and transforaminal, should be used only in the presence of radiculopathy. A multi-disciplinary or collaborative comprehensive evaluation is recommended before initiating treatment with epidural steroid injection. Epidural injections are indicated for the following patients:</p> <ul style="list-style-type: none"> <li>• Radicular pain resistant to more conservative measures or when surgery is contraindicated</li> <li>• Post-decompressive radiculitis or post-surgical scarring</li> <li>• Monoradicular pain, confirmed by diagnostic block in which a surgically correctible lesion cannot be identified</li> <li>• Treatment of acute herpes zoster or post herpetic neuralgia</li> </ul> <p>Patients must meet the following conditions for epidural injection to be considered medically necessary:</p> <ul style="list-style-type: none"> <li>• Epidural injections should not exceed a series of three per spinal region in a six-month period. They may be performed at intervals of one week or greater.</li> <li>• With each subsequent injection the medical record should clearly document the interval effect(s) from the prior injection.</li> <li>• If two injections have not provided improvement in pain or functional status, a third injection should not be given unless a compelling technical reason is present.</li> <li>• Fluoroscopic guidance must be used for single nerve root/transforaminal injections to ensure proper needle placement.</li> <li>• Injections for chronic pain that are not performed under imaging (fluoroscopy or CT) guidance are not considered medically necessary</li> </ul> <p><u>Facet joint injection:</u> Facet joint injections are considered medically necessary for the treatment of chronic pain that has failed to respond to more conservative treatment. Radiculopathy should be ruled out before proceeding with facet joint injection. Providing more than three levels of facet joint blocks on the same day is not considered medically necessary.</p> <ul style="list-style-type: none"> <li>• No more than four injections per region per patient should be administered in a one year period.</li> <li>• Facet joint injections not performed under the guidance of fluoroscopy or</li> </ul>	<p>62319, 64479, 64480, 64483, 64484, 77003, 77012, 64490, 64491, 64492, 64493, 64494, 64495</p>

Payer (Year)	Lit search dates	Evidence base available	Policy	Rationale / comments
			CT imaging are not considered medically necessary.	
BCBS Regence Group (ID, OR, UT, much of WA) Medical Policy: Facet Joint Injections (135) (2009)	Through 7/2008	Facet joint injection: 1 practice guideline (ASIPP)  1 pilot study (Hyaluronic acid only)	<p><u>Facet joint injection</u>: Therapeutic facet joint injection may be covered when performed under fluoroscopy for the management of chronic neck or back pain (pain lasting at least three months despite conservative treatment such as physical therapy and non-steroidal anti-inflammatory medication). Facet joint injections for the treatment of acute back or neck pain are not considered medically necessary. Patients must meet the following criteria for injections to be considered medically necessary:</p> <ul style="list-style-type: none"> <li>• One injection per level per side every two months or longer provided the patient has achieved at least 50% pain relief in six weeks. The medical record must clearly document responsiveness to prior injections indicating improvement in physical and functional status;</li> <li>• Injections are limited to a maximum of six per year;</li> <li>• A maximum of 16 injections in a lifetime is rarely considered medically necessary.</li> </ul> <p>Exceptions to the lifetime limit include:</p> <ul style="list-style-type: none"> <li>• Pathology involving both cervical and lumbar spine;</li> <li>• Bilateral facet joint injections;</li> <li>• Recurrence of symptoms at least two years after previous successful facet joint injection treatments.</li> </ul> <p>Injection of viscosupplementation agent (Hyaluronic acid) is considered investigational.</p>	CPT codes if conditions are met: 64490, 64491, 64492, 64493, 64494, 64495, 77003, 0213T, 0214T, 0215T, 0216T, 0127T, 0128T

AAN: American Academy of Neurology  
 AANS: American Association of Neurological Surgeons  
 ACOEP: American College of Occupational and Environmental Medicine  
 AHRQ: Agency for Healthcare Research and Quality  
 APS: American Pain Society  
 ASA: American Society of Anesthesiologists  
 ASIPP: American Society of Interventional Pain Physicians  
 CADTH: Canadian Agency for Drugs and Technologies in Health  
 ICSI: Institute for Clinical Systems Improvement  
 NASS: North American Spine Society  
 NR: not reported

## 3. The Evidence

### 3.1. *Methods of the Systematic Literature Review*

The primary aim of this assessment was to systematically review, critically appraise and analyze research evidence evaluating the efficacy, effectiveness, safety, and predictive factors for using spinal injections for the treatment of subacute or chronic spinal pain.

A large body of literature exists on lumbar spinal injections, including many recent systematic reviews. We reviewed a number of systematic reviews and elected to use as a baseline of evidence the one conducted by Chou et al (2009)<sup>39, 40</sup> at the Oregon Evidence-Based Practice Center. We chose this systematic review as our baseline for three reasons: (1) The systematic review was comprehensive and included all lumbar injections that were germane to our report. (2) It was of high quality (see the critical appraisal in section 3.2.2). (3) There is available an associated Evidence Report<sup>40</sup> that contained added information useful to our Assessment. Other systematic reviews are summarized in section 2.9. We accepted the results of the baseline review, and then we included all randomized controlled trials published since the July 2008 search conducted in the baseline systematic review. For the lumbar portion of Key Question 1, we included only RCTs following the decision of Chou et al. For the cervical portion, we included all published RCTs. For Key Question 2, we included RCTs, controlled observational studies and large case series ( $N \geq 100$ ) that evaluated harms. For Key Question 3, RCTs and prognostic cohort studies were included. Studies of cost were included if they were a full economic analysis (cost-effectiveness, cost-minimization, or cost-utility study) to answer Key Question 4.

#### 3.1.1. Inclusion/exclusion

Inclusion and exclusion criteria are summarized in Table 4.

- **Population.** Studies of adults who underwent lumbar or cervical spinal injections for the treatment of subacute or chronic spinal pain due to conditions including (but not limited to) degenerative disc disease (DDD), sciatica, radiculopathy, disc herniation, spinal stenosis, failed back surgery syndrome (FBSS), facet joint pain, or sacroiliac joint pain. Studies in which more than 25% of patients had the following diagnoses were excluded: acute major trauma, cancer, infection, cauda equina syndrome, fibromyalgia, spondyloarthropathy, or osteoporosis.
- **Intervention.** Included studies that evaluated therapeutic lumbar or cervical spinal injections, including: epidural injections, intraarticular facet injections, medial branch blocks, intradiscal injections, and sacroiliac joint injections. Studies reporting on diagnostic injections, extraspinal injections, chemonucleolysis, or radiofrequency denervation, intradiscal electrothermal therapy, coblation nucleoplasty and related procedures were excluded.
- **Comparator.** Included studies that compared spinal injections to placebo (saline/water and/or local anesthetic) injections or to non-placebo controls were included.
- **Outcomes.** Eligible studies reported on at least one of the following outcomes: pain, physical function, quality of life, patient satisfaction, opioid use, return to work, any other reported surrogate, and complications (including but not limited to mortality, major morbidity, dural or arachnoid puncture, infection, hematoma, allergic reaction, nerve or spinal cord injury, artery/vein damage/puncture, and arachnoiditis). Studies reporting on non-clinical outcomes were excluded.
- **Study design.** For key question 1, eligible studies compared spinal injections with placebo or non-placebo injections utilizing a randomized study design. In order to provide additional context for key

question 2, case series with  $\geq 100$  patients and registry studies were sought. For key question 3, we considered comparative clinical studies that evaluated prognostic factors (including but not limited to injection approach, injectate characteristics, gender, age, psychological or psychosocial comorbidities, diagnosis or duration of disease, provider type or other provider characteristics) associated with differential efficacy or safety of spinal injections. Formal cost-effectiveness economic analyses published in peer-reviewed journals were eligible for inclusion to help answer key question 4.

**Table 4. Summary of inclusion and exclusion criteria**

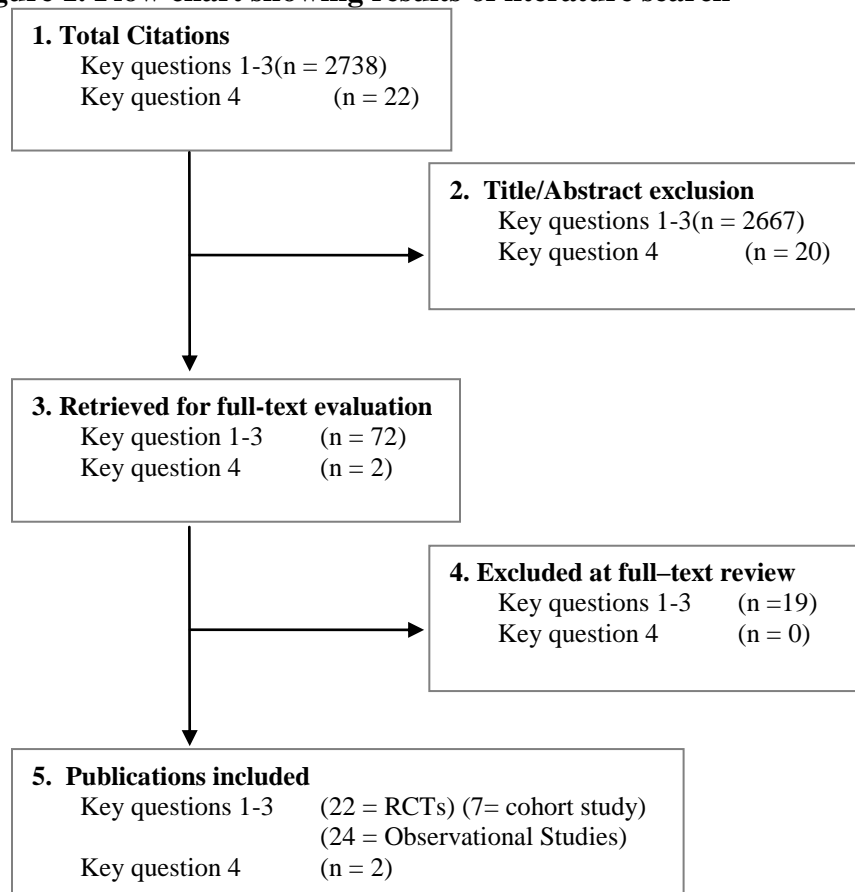
Study Component	Inclusion	Exclusion
<b>Participants</b>	Adults with: ♦ Cervical or lumbar sub-acute or chronic spinal pain	♦ Children ♦ Acute major trauma ♦ Cancer ♦ Infection ♦ Cauda equina syndrome ♦ Fibromyalgia ♦ Spondyloarthropathy ♦ Osteoporosis ♦ Vertebral compression fracture
<b>Intervention</b>	Lumbar or cervical intraspinal injections to include: ♦ Epidural injections ♦ Facet joint injections ♦ Medial branch block ♦ Sacroiliac joint injections ♦ Intradiscal injections	♦ Extraspinal injections (Botulinum toxin injections, local injections, prolotherapy) ♦ Chemonucleolysis ♦ Radiofrequency denervation, intradiscal electrothermal therapy, coblation nucleoplasty and related procedures
<b>Comparators</b>	♦ Placebo or active control	
<b>Outcomes</b>	♦ Pain ♦ Physical function ♦ Health-related quality of life ♦ Patient satisfaction ♦ Opioid use ♦ Complications and adverse effects (e.g. procedural complications and technical failures).	♦ Non-clinical outcomes
<b>Study Design</b>	♦ Randomized controlled trials (RCTs) will be sought for key question 1 ♦ Case series designed to report complications with $N \geq 100$ and registry studies will be sought for key question 2 ♦ Comparative clinical studies (e.g. RCTs, cohort studies with concurrent controls) will be considered for key question 3 ♦ Formal economic studies will be sought for question 4	♦ Case series other than those with $N \geq 100$ for key question 2 ♦ Case reports other than for context ♦ Non-clinical studies (e.g., technical reports) ♦ Studies in which $< 75\%$ (or an unreported percentage) of patients have any of the excluded diagnoses (see above)
<b>Publication</b>	♦ Studies published in English in peer reviewed journals, published HTAs or publicly available FDA reports ♦ Full formal economic analyses (e.g. cost-utility studies) published in English in an HTA, or in a peer-reviewed journal published after those represented in previous HTAs.	♦ Abstracts, editorials, letters ♦ Duplicate publications of the same study which do not report on different outcomes ♦ Single reports from multicenter trials ♦ Studies reporting on the technical aspects spinal injections ♦ White papers ♦ Narrative reviews ♦ Articles identified as preliminary reports when results are published in later versions ♦ Incomplete economic evaluations such as costing studies

### 3.1.2. Data sources and search strategy

The clinical studies included in this report were identified using the algorithm shown in Appendix A. The search took place in four stages. The first stage of the study selection process consisted of a comprehensive literature search using electronic means and hand searching. We then screened all possible relevant articles using titles and abstracts in stage two. This was done by two individuals independently. Those articles that met a set of *a priori* retrieval criteria based on the criteria above were included. Any disagreement between screeners that were unresolved resulted in the article being included for the next stage. Stage three involved retrieval of the full text articles remaining. The final stage of the study selection algorithm consisted of the selection of those studies using a set of *a priori* inclusion criteria, again, by two independent investigators. Those articles selected form the evidence base for this report.

Electronic databases searched included PubMed, EMBASE, CINAHL, ClinicalTrials.gov, CRISP, HSTAT, *The Cochrane Library*, EconLIT, PsychINFO, AHRQ, and INAHTA for eligible studies, including health technology assessments (HTAs), systematic reviews, primary studies and FDA reports. The databases were searched from inception through August, 2010. Reference lists of all eligible studies were also searched. The search strategies used for PubMed and EMBASE, are shown in Appendix B. Figure 1 shows a flow chart of the results of all searches for included primary studies. Articles excluded at full-text review are listed in Appendix C.

**Figure 1. Flow chart showing results of literature search**



### 3.1.3. Data extraction

Reviewers extracted the following data from the clinical studies: study population characteristics, study type, study period, patient demographics and preoperative diagnoses, study interventions, follow-up time, study outcomes (pain, patient satisfaction, global perceived effect, health-related quality of life, anxiety and depression, function, medication usage, and “success”), adverse events (reoperation, device-related complications, and other complications or side effects). An attempt was made to reconcile conflicting information among multiple reports presenting the same data. For key question 1, the APS/Chou evidence report<sup>39, 40</sup> was used as a basis for lumbar spinal injections; thus we accepted the conclusions of this report and did not abstract data from the studies included in that report. For economic studies, data related to sources used, economic parameters and perspectives, results, and sensitivity analyses were abstracted.

### 3.1.4. Study quality assessment: Level of evidence (LoE) evaluation

The method used by Spectrum Research, Inc.(SRI) for assessing the quality of evidence of individual studies as well as the overall quality of evidence incorporates aspects of the ratingscheme developed by the Oxford Centre for Evidence-based Medicine<sup>162</sup>, precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group<sup>12</sup>, and recommendations made by the Agency for Healthcare Research and Quality (AHRQ)<sup>215</sup>.

Details of the Level of Evidence (LoE) methodology are found in Appendix E. Each clinical/human study chosen for inclusion was given a LoE rating based on the quality criteria listed in Appendix D. Standardized abstraction guidelines were used to determine the LoE for each study included in this assessment.

## **3.2. *Quality of Literature available***

### **3.2.1. Quality of studies retained**

We initially found 2738 citations using the search strategy in Appendix B.

For Key Question 1 we identified 26 RCTs that compared spinal injections with placebo or non-placebo controls. From among these, 19 RCTs met our inclusion criteria. Eighteen RCTs are graded as LoE IIb; one RCT received the LoE grade of IIa. Critical appraisals of the RCTs and cohort study are included in section 3.2.3. For lumbar spinal injections, we only included RCTs published after the APS/Chou systematic review's literature search was conducted (mid-2008)<sup>39, 40</sup>.

For Key Question 2 on safety, we included in addition to the studies cited in the preceding paragraph, 14 case series with  $N \geq 100$ . We also reviewed conclusions from ten additional case series, five of which evaluated the incidence of intravascular puncture, and five of which assessed radiation exposure to the physician. All the case series received the LoE grade of IV.

To address prognostic factors associated with differential efficacy or safety following spinal injections (Key Question 3), we included four RCTs, one prospective and six retrospective cohort studies. The RCTs received the LoE grade of IIb, and all of the cohort studies received the LoE grade of III.

### 3.2.2. Critical appraisal of systematic reviews

**Chou et al (2009) Evidence Report/Systematic Review for the American Pain Society<sup>39, 40</sup>** (see also Appendix E)

- Purpose, aim, study question and/or hypothesis: The evidence report was commissioned by the American Pain Society to review the evidence for the management of acute and chronic low back pain. The key question relevant to spinal injections asked: how effective are injection procedures (and different injection interventions) and other interventional therapies for non-radicular low back pain, radicular low back pain, or spinal stenosis, and under what circumstances? Spinal injections fell under the category of invasive, non-surgical interventions, and (as relevant to the scope of this report) included epidural steroid injections, intradiscal steroid injections, facet (zygapophysial) joint injections, therapeutic medial branch blocks, and sacroiliac joint steroid injections. In addition, the cost-effectiveness of different interventions was assessed.
- Literature search: Studies were identified using defined search methods; search dates ranged from studies published between 1966 and July 2008.
- Unpublished sources did not appear to have been sought, although electronic searches were supplemented by hand-searching bibliographies and assessing studies suggested by experts (no further details provided).
- Inclusion/exclusion criteria: Inclusion criteria (as relevant to the scope of this report): controlled clinical trials and systematic reviews, controlled observational studies for the assessment of adverse events only, studies of cost if they were conducted alongside a randomized trial or were a full economic analysis (cost-effectiveness, cost-minimization, or cost-utility study), English language trials, and studies that included adult, non-pregnant patients with low back pain of any duration with or without leg pain and reported on one or more of the following outcomes: back-specific function, generic health status, pain, work disability, or patient satisfaction. Exclusion criteria (as relevant to the scope of this report): outdated systematic reviews (published before the year 2000), observational studies, non-English trials (unless they were already included in English-language systematic reviews), studies of non-human subjects and those without original data, conference abstracts, and studies that evaluated patients with acute major trauma, cancer, infection, *cauda equina* syndrome, fibromyalgia, spondyloarthropathy, osteoporosis, or vertebral compression fracture.
- Characteristics of included studies provided: Information was provided with regard to study design (RCTs), populations studied (diagnosis), and technologies applied (injection type).
- Quality of included studies formally assessed: The internal validity of trials and systematic reviews was graded by two independent reviewers using the Cochrane Back Review Group<sup>205</sup> criteria and the methods developed by Oxman and Guyatt<sup>157</sup>, respectively. Studies that received more than half of the maximum possible quality score were considered to be “higher-quality” for any quality rating system used.
- Quantitative analysis:
  - Studies were appraised critically, as described above.
  - The magnitude and direction of effect sizes were determined by assessing the magnitude of benefits or harms. For pain relief and functional status, mean differences in effects were considered small/modest if they ranged between 5-10 points (on a 100 point VAS scale or in ODI scores, respectively), moderate if they fell between 10-20 points, and large/substantial if they were greater than 20 points.

- The consistency of effect sizes was evaluated by grading conclusions. Interventions that were beneficial were classified as positive, those that were harmful or not beneficial were classified as negative, and those for which more than 25% of higher-quality studies (or two or more higher-quality systematic reviews) reached different conclusions (positive or negative) were classified as inconsistent.
- The stability of effect sizes was considered in the reporting of confidence intervals, missing data and study sample size.
- The scientific quality of studies was considered in the conclusions. An overall strength of evidence was assigned for each comparison and outcome evaluated using methods adapted from the U.S. Preventative Services Task Force. A rating of good quality indicated that evidence was consistent and obtained from at least two higher-quality RCTs; this rating suggested that there was a high degree of certainty that the results are true. A rating of fair quality was assigned if the evidence was adequate to determine the effects on health outcomes but was limited by the number, quality, size, or consistency of the included studies; this rating could be attributed to true effects or bias in at least some of the studies. A rating of poor quality was given if the evidence was not sufficient to determine the effects on health outcomes due to limited number (i.e., < 2 studies) or power of studies, large or unexplained inconsistency of results between higher-quality trials or significant flaws in trial design or conduct; this rating indicated that reliable conclusions could not be made.
- Methods to enhance objectivity were incorporated, as described above (consistency of effect sizes, scientific quality of studies).
- Qualitative analysis:
  - Heterogeneity was evaluated as part of the consistency of effect sizes, above, though there was no apparent heterogeneity in the studies evaluating spinal injections.
  - Effect sizes were not pooled using actual numbers, however the magnitude and direction of effect sizes were evaluated as described above.
  - Sensitivity analysis was explored through analysis stratified by study quality and type of control treatment for epidural spinal injections. There were too few placebo controlled trials for facet joint, medial branch nerve, intradiscal and sacroiliac joint injections to provide meaningful sensitivity analysis.
- Conflict of interest: Neither of the investigators had a conflict of interest.

Recently, Manchikanti et al (2010)<sup>128</sup> published a critical review of the American Pain Society's evidence report of therapeutic interventions for spinal pain. A summary of this review is included in Appendix F.

Dr. Chou's rebuttal to Dr. Manchikanti's review can be found in Appendix G.

### **3.2.3. Critical appraisal of randomized controlled trials**

#### **Lumbar injections**

##### **Lumbar epidural injections**

All twelve studies received a level of evidence (LoE) grade of I Ib (Appendix E).

*Manchikanti studies*<sup>115-118, 132-134, 136</sup>.

Manchikanti et al published eight RCTs since 2008 that were included in the evaluation of the efficacy of lumbar epidural steroid injections. These studies all used similar methodology.

- **Sample size:** Across the eight studies, sample sizes ranged from 61 to 180 patients randomized. Each study included only a proportion of patients randomized (range, 58-70%), which consisted of the first consecutive X number of patients who had completed one year follow-up (personal correspondence with Dr. Manchikanti, see Appendix H). For example, in Manchikanti (2009)<sup>134</sup> (A comparative effectiveness...), 180 patients were randomized. Three and a half years later, 126 patients had completed one year follow-up. The authors decided to include the first 60 consecutive patients in each group.
- **Randomization and concealed allocation:** Randomization was achieved using computer-generated random allocation sequences. The nursing coordinators enrolled patients and assigned participants to their respective groups. Whether the treatment was concealed to the nurses is not clear. The operating room nurse prepared the injections. Although the physicians performing the injections were blinded to the treatment assignment and study participation status of each patient, no information was given as to how concealment of patient allocation was ensured prior to the procedure.
- **Intention to treat:** Credit for intention to treat analysis was not given in six<sup>115, 117, 118, 132-134</sup> of the studies as patients who crossed over to the other treatment for subsequent injections could do so only after unblinding and hence withdrawal from the study. Credit for intention to treat analysis was given in the remaining two<sup>116, 136</sup> studies; there was no indication that patients had the option to change treatment and no patients were unblinded or withdrawn.
- **Blinding:** There was no indication that the physician who recorded patient outcomes was blinded. The major outcomes (pain, function, opioid use, and employment status) were all patient-reported. In cases where the patient remained blinded to treatment, patient reported assessment of outcomes was considered blinded.
- **Cointerventions:** The cointerventions were not equally applied since additional treatments received by patients (i.e., physical therapy, occupational therapy, bracing, etc.) were permitted but not controlled for or reported (except for opioid usage).
- **Length of follow-up and percent of patients followed:** The follow-up period was twelve months in all studies. However, data collected following the three-<sup>115, 133, 134</sup> or six-<sup>117</sup> month follow-ups were excluded in a total of four studies: more than 20% of the data reported for either group were carried forward from the last available follow-up as a result of unavailable data or patient withdrawal. None of the studies had complete follow-up of 80% or more (range, 38-62% complete follow-up) since not all patients randomized were included in the study.
- **Confounding:** Confounding was controlled for in four studies<sup>115, 117, 118, 133</sup>; the other four studies<sup>116, 132, 134, 136</sup> had potentially meaningful differences between study groups at baseline that were not controlled for in the analysis.
- **Conflict of interest:** All studies contained a statement that there was no conflict of interest and that no external funding was received for the preparation of the manuscripts. Dr. Manchikanti is the chief executive officer, founder, and chairman of the board of ASIPP (American Society of Interventional Pain Physicians; <http://www.asipp.org/>)<sup>11</sup> and the chief executive officer and chairman of the board of SIPMS (the Society of Interventional Pain Management Surgery Centers; <http://www.sipms.org/>)<sup>181</sup>. More information on these organizations may be found in Appendix I.

*Sayegh (2009)*<sup>176</sup>

- **Sample size:** One-hundred eighty-three patients were randomized to receive caudal epidural injections with local anesthetic and either steroids (n = 93) or water (n = 90).
- **Randomization and concealed allocation:** No information was reported as to the method of randomization, and there was no mention of concealment.

- Intention to treat: Although it was not explicitly stated that the intention to treat principle was used, data appear to have been analyzed in this manner: patients receiving additional injections received the same preparation originally used; patients were excluded from analysis only if they decided to undergo operative treatment after inadequate relief following second injection.
- Blinding: The patients, surgeons, and the evaluating physician were all blinded to the patient's intervention.
- Cointerventions: We did not consider cointerventions to have been equally applied as no information was given regarding the types of additional treatments pain patients are likely to receive (i.e., physical therapy, occupational therapy, bracing, etc.); although all patients received the same medications during the first four weeks, opioid usage for the remainder of the follow-up period (one year) was not reported.
- Length of follow-up and percent of patients followed: Patients were followed for one year; 83% of patients had complete follow-up. Data were also collected at one week, one month, and six months.
- Confounding: Confounding was controlled for: there were no potentially meaningful differences in a variety of baseline characteristics between groups.
- Conflict of interest: None. The authors did not receive any funds to support this work or receive any benefits as a result of the study.

*Ghahreman (2010)<sup>64</sup>*

- Sample size: Patients (N = 150) were randomized to receive one of five treatments: transforaminal injections with (1) steroids and local anesthetic (n = 28) or (2) local anesthetic (n = 27) or (3) saline (n = 37) or intramuscular injections with (4) local anesthetic (n = 28) or (5) saline (n = 30).
- Randomization and concealed allocation: Randomization was achieved using a series of random numbers allocated sequentially to patients as they enrolled; a research nurse carried out the randomization process. The nurse provided allocation information via printed card to the operator during the procedure. No information was provided on how concealment was ensured throughout the study process.
- Intention to treat: At one month follow-up (primary outcome reported here), data for all patients were analyzed according to the treatment assigned.
- Blinding: The patients and surgeon were blinded to the treatment procedure; the primary outcomes were patient-reported. Follow-up assessments were performed by the senior author or a research nurse: both were blinded and neither conducted the treatment.
- Cointerventions: No restrictions were placed on the use of other health care (opioids, analgesics and non-steroidal anti-inflammatory drugs, or physical therapy). Data on use before and after treatment was only provided for those patients with successful treatment at one month, therefore, credit could not be given.
- Length of follow-up and percent of patients followed: Pain data were reported at one month (100% follow-up). Between three and twelve months, the authors reported on data only for those patients with treatment success at one month and thus the follow-up was  $\leq 25\%$ , making the three to twelve month data difficult to interpret.
- Confounding: Confounding was not controlled for as there were potentially meaningful differences in some of the baseline characteristics between groups that were not controlled for (patients receiving transforaminal steroids had a longer duration of chronic pain compared with those who received intramuscular steroids; other differences in baseline characteristics were reported between the four different control groups).

- Conflict of interest: not reported.

*Tafazal (2009)<sup>197</sup>*

- Sample size: Patients (N = 150) were randomized to receive peri-radicular injections (around the nerve root) (equivalent to transforaminal epidural injections) with anesthetic alone (n = 76) or with steroids (n = 74).
- Randomization and concealed allocation: Randomization was achieved using a table of random numbers. Although care was taken to conceal the treatment agents during the procedure, no information was provided on how concealment was ensured in the period after allocation and prior to the procedure.
- Intention to treat: Credit was not given since patients receiving additional injections or surgeries were excluded from analysis.
- Blinding: The patients and surgeon were blinded to the treatment procedure; the primary outcomes were patient-reported.
- Cointerventions: Patients were instructed to continue their pretreatment medication schedule and prohibited from undergoing any sort of additional therapy during the follow-up period. Any differences in the pretreatment medication schedules are expected to be accounted for as a result of the randomization process.
- Length of follow-up and percent of patients followed: Pain and function data were reported at 12 weeks (83% follow-up); the need for additional nerve blocks or surgeries was reported at one year (86% follow-up).
- Confounding: Confounding was controlled for as there were no meaningful differences in a variety of baseline characteristics between groups.
- Conflict of interest: not reported.

*Koc (2009)<sup>99</sup>*

- Sample size: Patients (N = 29) were randomized to receive interlaminar epidural steroid/local anesthetic injections (n = 10), conservative inpatient physical therapy alone (n = 10), or control (n = 9; presumably no treatment, intervention not described).
- Randomization and concealed allocation: The method by which patients were randomized was not reported; there was no mention of concealment.
- Intention to treat: There was no explicit statement that the intention to treat principle was used, however, data appear to have been analyzed in this manner.
- Blinding: The patients and surgeons could not be blinded due to differences in treatment interventions. Although the investigator who evaluated patients was blinded, because the primary outcomes (VAS, Roland-Morris Disability Index, and Nottingham Health Profile) were all patient-reported and patients were not blinded, we did not give credit for blinding.
- Cointerventions: All patients received instructions on a therapeutic exercise program, which was to be performed twice daily for six months; all patients received the same medication for the first two weeks.
- Length of follow-up and percent of patients followed: Pain and function data were reported at 6 months (88% follow-up); data were also reported at 2 weeks, one month, and three months.
- Confounding: Confounding was not considered to have been controlled for as there was not a robust description of baseline characteristics.
- Conflict of interest: None. The authors did not receive any funds to support this work or receive any benefits as a result of the study.

### Lumbar facet interventions

One RCT was identified and received a LoE grade of IIb (Appendix E).

*Manchikanti (2010)<sup>135</sup> (Evaluation of lumbar...):*

- Sample size: Although 120 patients were randomized, only 84 (70%) were included in the study.
- Randomization and concealed allocation: Randomization was achieved using computer-generated random allocation sequences in blocks of 20. The nursing coordinators enrolled patients and assigned participants to their respective groups. Whether the treatment was concealed to the nurses is not clear. The operating room nurse prepared the injections. Although the physicians performing the injections were blinded to the treatment assignment and study participation status of each patient, no information was given as to how concealment of patient allocation was ensured prior to the procedure.
- Intention to treat: Credit for intention to treat analysis was not given because patients had the option to be unblinded; nine patients total were unblinded due to lack of response. The authors did not report whether these patients had the option of receiving the alternative treatment.
- Blinding: Although there was no indication that the physician who recorded patient outcomes was blinded, the major outcomes (pain, function, opioid use, and employment status) were all patient-reported.
- Cointerventions: Cointerventions were not considered to have been equally applied since additional treatments received by patients (i.e., physical therapy, occupational therapy, bracing, etc.) were permitted but not controlled for or reported (except for opioid usage).
- Confounding: Confounding was controlled for since there were no differences in a variety of baseline characteristics between groups.
- Length of follow-up and percent of patients followed: The follow-up period was 24 months; there was an 80% complete follow-up rate at 24 months. Data were also collected at 3, 6, and 12 months; data collected at the 18 month follow-up only were excluded as more than 20% of the data reported for either group were carried forward from the last available follow-up as a result of unavailable data or patient withdrawal.
- Conflict of interest: The study contained a statement that there was no conflict of interest and no external funding was received for the preparation of the manuscripts. More information on Dr. Manchikanti's affiliation with ASIPP (American Society of Interventional Pain Physicians; <http://www.asipp.org/>)<sup>11</sup> and SIPMS (the Society of Interventional Pain Management Surgery Centers; <http://www.sipms.org/>)<sup>181</sup> may be found in Appendix I.

**Sacroiliac joint injections**- no additional studies were identified.

### Lumbar intradiscal injections

One RCT was identified and received a LoE grade of IIa (Appendix E).

*Peng (2010)<sup>161</sup>*

- **Sample size:** A total of 72 patients were randomized to receive lumbar intradiscal injections with methylene blue (neurolytic agent)/local anesthetic (n = 36) or saline/local anesthetic (n = 36).
- **Randomization and concealed allocation:** Patients were randomized using a table of random numbers according to a 1:1 randomization schedule. While the treatment allocations were contained within sealed envelopes, there was no mention as to the opacity of the envelopes and thus we did not give credit.
- **Intention to treat:** There was no explicit statement that the intention to treat principle was used, however, data appear to have been analyzed in this manner. No mention was made of repeat injections.
- **Blinding:** While the operating surgeon was not blinded due to color differences in the injectates, both the patients and the physician who evaluated patient outcomes were blinded.
- **Cointerventions:** Cointerventions were considered to have been equally applied since postoperative instructions were the same and the injecting physician did not participate in follow-up.
- **Length of follow-up and percent of patients followed:** Pain and function data were reported at 24 months (99% follow-up); data were also reported at 6 and 12 months.
- **Confounding:** Confounding was controlled for since there were no differences between groups in a variety of characteristics at baseline.
- **Conflict of interest:** The authors stated no conflict of interest; the work was supported by grants from the 304<sup>th</sup> Hospital and the Foundation of Capital Medical Development in Beijing.

### **Cervical injections**

#### **Cervical epidural injections**

Three studies were identified and received a LoE grade of IIb (Appendix E).

*Manchikanti (2010)*<sup>124, 125</sup>

Manchikanti et al published two RCTs in which outcomes following cervical epidural steroid injections were evaluated. These studies all used similar methodology.

- **Sample size:** A total of 120 patients were randomized in each study, however each study reported data for only 58% of the patients randomized.
- **Randomization and concealed allocation:** Randomization was achieved using computer-generated random allocation sequences. The nursing coordinators enrolled patients and assigned participants to their respective groups. Whether the treatment was concealed to the nurses is not clear. The operating room nurse prepared the injections. Although the physicians performing the injections were blinded to the treatment assignment and study participation status of each patient, no information was given as to how concealment of patient allocation was ensured prior to the procedure.
- **Intention to treat:** Credit for intention to treat analysis was not given in one<sup>124</sup> of the studies because one patient was unblinded (and hence withdrawn); additional injections were provided after unblinding or without unblinding, and it is not stipulated that patients who were unblinded could not receive the opposite treatment. Credit for intention to treat analysis was given in the second study<sup>125</sup> since no patients were unblinded.
- **Blinding:** Although there was no indication that the physician who recorded patient outcomes was blinded, the major outcomes (pain, function, opioid use, and employment status) were all patient-reported.

- Cointerventions: The cointerventions were not equally applied since additional treatments received by patients (i.e., physical therapy, occupational therapy, bracing, etc.) were permitted but not controlled for or reported (except for opioid usage).
- Length of follow-up and percent of patients followed: Both studies reported data out to twelve months' follow-up; data was also collected at three and six months. Neither study had complete follow-up of 80% or more (56% complete follow-up in both) since not all patients randomized were included in the study.
- Confounding: Confounding was controlled for in both studies as there were no differences in the baseline characteristics between groups.
- Conflict of interest: Both studies contained a statement that there was no conflict of interest and no external funding was received for the preparation of the manuscripts. More information on Dr. Manchikanti's affiliation with ASIPP (American Society of Interventional Pain Physicians; <http://www.asipp.org/>)<sup>11</sup> and SIPMS (the Society of Interventional Pain Management Surgery Centers; <http://www.sipms.org/>)<sup>181</sup> may be found in Appendix I.

*Stav (1993)*<sup>193</sup>

- Sample size: Fifty patients were randomized, however the number of patients allocated to each group was not reported prior to loss to follow-up.
- Randomization and concealed allocation: No information was provided regarding the method of randomization or whether the group allocations were concealed.
- Intention to treat: There was no explicit statement that the intention to treat principle was used, however, data appear to have been analyzed in this manner.
- Blinding: No mention was made of blinding of patients or evaluating physicians.
- Cointerventions: Patients were instructed to continue their pretreatment medication schedule. Any differences are expected to be accounted for as a result of the randomization process.
- Length of follow-up and percent of patients followed: Data was reported at one week and twelve months; the complete follow-up rate was 84%.
- Confounding: Confounding was controlled for since there were no differences between groups in a variety of characteristics at baseline.
- Conflict of interest: not reported.

### Cervical facet interventions

Two RCTs were identified, both of which received a LoE grade of IIb (Appendix E).

*Manchikanti (2006/2008)(two different reports of the same study)*<sup>126, 137</sup>

- Sample size: A total of 120 patients were randomized (n = 60 per treatment group).
- Randomization and concealed allocation: Randomization was achieved using computer-generated random allocation. The nursing coordinators enrolled patients and assigned participants to their respective groups. Whether the treatment was concealed to the nurses is not clear. The operating room nurse prepared the injections. Although the physicians performing the injections were blinded to the treatment assignment and study participation status of each patient, no information was given as to how concealment of patient allocation was ensured prior to the procedure.
- Intention to treat: Credit for intention to treat analysis was given (no patients were unblinded).

- **Blinding:** Although there was no indication that the physician who recorded patient outcomes was blinded, the major outcomes (pain, function, opioid use, and employment status) were all patient-reported.
- **Cointerventions:** The cointerventions were not equally applied since additional treatments received by patients (i.e., physical therapy, occupational therapy, bracing, etc.) were permitted but not controlled for or reported (except for opioid usage).
- **Length of follow-up and percent of patients followed:** Patients were followed for twelve months; data was also reported at three and six months. The complete follow-up rate was 88%.
- **Confounding:** Confounding was controlled for: there were no differences in the baseline characteristics between groups.
- **Conflict of interest:** The study contained a statement that there was no conflict of interest and no external funding was received for the preparation of the manuscripts. More information on Dr. Manchikanti's affiliation with ASIPP (American Society of Interventional Pain Physicians; <http://www.asipp.org/>)<sup>11</sup> and SIPMS (the Society of Interventional Pain Management Surgery Centers; <http://www.sipms.org/>)<sup>181</sup> may be found in Appendix I.

*Barnsley (1994)<sup>15</sup>*

- **Sample size:** Forty-two patients were randomized.
- **Randomization and concealed allocation:** A table of random numbers was used for treatment allocation, however, the authors did not report whether the treatment assignments were concealed.
- **Intention to treat:** There was no explicit statement that the intention to treat principle was used, however, data appear to have been analyzed in this manner.
- **Blinding:** Follow-up data were collected by an observer who was blinded to the patients' treatments.
- **Cointerventions:** Patients were instructed to continue their pretreatment medication and physical therapy schedule. Any differences are expected to be accounted for as a result of the randomization process.
- **Length of follow-up and percent of patients followed:** Patients were followed for up to 36 weeks, 98% of patients had complete follow-up.
- **Confounding:** Confounding was controlled for since there were no differences between groups in a variety of characteristics at baseline.
- **Conflict of interest:** The work was supported by a grant from the Motor Accidents Authority of New South Wales, Australia.

### **Cervical intradiscal injections**

No studies were identified.

## 4. Results

### 4.1. Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?

#### Lumbar spinal injections

##### 4.1.1. Lumbar interlaminar or caudal epidural injections versus placebo (saline/water and/or local anesthetic) controls

##### *Low back pain with sciatica or radiculopathy*

RCTs/SRs ≤ 2008: Chou et al (2009)<sup>39, 40</sup> concluded that there was inconsistent evidence that lumbar epidural steroid injections were beneficial based on results from 17 placebo-controlled RCTs (Table 5).

- *Short-term (≤ 3 months): results were mixed.* Of the seventeen trials reporting, 41% (7/17) showed a benefit in pain and function outcomes (positive results) following epidural steroid injections; two of these trials were graded as higher-quality while five were considered lower-quality. Another 41% of studies reported no benefit or harmful effects following epidural steroid injections (negative results); three were considered to be higher-quality and four were lower-quality. Results were unclear (p-values not reported) in 18% (3/17) of studies, all of which were lower-quality.
  - Stratification by type of placebo injection (epidural versus non-epidural) yielded clearer results: results were positive in 27% (3/11) of epidural-controlled and in 67% (4/6) of non-epidural (primarily interspinous ligament injections) controlled trials.
  - Stratification of trials by study quality had no effect on the consistency of results.
- *Long-term (> 3 months): there was no benefit* associated with lumbar epidural steroid injections (negative results). Seven of nine (78%) studies found no benefit or a harmful effect (negative results), however only two of these studies were higher-quality. One (11%) lower-quality trial found a beneficial outcome following lumbar epidural steroid injections, and another lower-quality study (11%) reported mixed results.

Three higher-quality systematic reviews were also identified<sup>110, 151, 208</sup>, and conclusions were mixed. A Cochrane review reported no benefit in short-term pain relief based on data from four trials<sup>151</sup>; a second systematic review reached the same conclusions (follow-up not reported) based on data from seven trials<sup>110</sup>. The third systematic review reported that epidural steroid injections were superior to placebo injections in symptom improvement in patients with sciatica<sup>208</sup>.

The overall quality of evidence (combined with transforaminal epidural injections) was considered to be fair.

RCTs ≥ 2008: We identified three additional RCTs<sup>132, 136, 176</sup> published after the APS systematic review. All studies received a LoE grade of IIb. Detailed demographic and outcome data are available in Appendix L.

Treatment (steroid) versus placebo (saline/water and/or local anesthetic) epidural injection:

- Short-term (≤ 3 months)
  - *Pain: there was no benefit* as reported by 100% of two studies<sup>132, 136</sup> at three months (Table 5):

- mean NRS scores (0-10 cm):
      - $3.4 \pm 1.7$  versus  $8.0 \pm 0.8$ , respectively (ns)<sup>132</sup>
      - $3.5 \pm 1.1$  versus  $3.9 \pm 1.2$ , respectively (ns)<sup>136</sup>
    - percent of patients achieving pain relief of 50% or more:
      - 81% versus 81%, respectively (ns)<sup>132</sup>
      - 86% versus 83%, respectively (ns)<sup>136</sup>
  - *Function: results were mixed*, with a benefit at one month and no benefit at three months (Table 5):
    - mean ODI scores (0-50 scale)
      - one month: *epidural steroids were superior*
        - $8.7 \pm 11.9$  versus  $23.5 \pm 9.6$ , respectively ( $P = .000$ )<sup>176</sup>
      - three months: *no benefit*
        - $13.8 \pm 6.3$  versus  $15.4 \pm 6.8$ , respectively (ns)<sup>132</sup>
        - $13.8 \pm 4.6$  versus  $15.4 \pm 5.2$ , respectively (ns)<sup>136</sup>
    - percent of patients achieving functional improvement by:
      - 40% or more: 79% versus 79%, respectively (ns)<sup>132</sup>
      - 50% or more: 80% versus 71%, respectively (ns)<sup>136</sup>
  - *Opioid use: there was no benefit* associated with lumbar epidural steroid injections in either of the two studies<sup>132, 136</sup> reporting this outcome at three months:
    - $27.4 \pm 20.4$  versus  $28.7$  versus  $15.5$  mg (morphine equivalents), respectively (ns)<sup>132</sup>
    - $40 \pm 36.1$  versus  $35 \pm 7.5$ , respectively (ns)<sup>136</sup>
- Long-term (> 3 months)
  - *Pain: there was no benefit* at twelve months in 100% (2/2) of studies<sup>132, 136</sup> reporting this outcome (Table 5):
    - mean NRS scores (0-10 cm):
      - $3.5 \pm 1.8$  versus  $3.7 \pm 1.4$ , respectively (ns)<sup>132</sup>
      - $3.3 \pm 1.2$  versus  $3.9 \pm 1.3$ , respectively (ns)<sup>136</sup>
    - percent of patients achieving pain relief of 50% or more:
      - 81% versus 79%, respectively (ns)<sup>132</sup>
      - 86% versus 74%, respectively (ns)<sup>136</sup>
  - *Length of pain relief (mean): there was no benefit:*
    - $35.9 \pm 15.4$  weeks versus  $35.2 \pm 17.2$  weeks, respectively (ns)<sup>132</sup>
    - $40.2 \pm 12.9$  versus  $35.3 \pm 18.1$  weeks, respectively (ns)<sup>136</sup>
  - *Function: results were mixed* at twelve months (Table 5).
    - mean ODI scores (0-50 scale): *results were mixed, with two of the three studies showing a benefit:*
      - $12.5 \pm 6.4$  versus  $14.1 \pm 6.9$ , respectively (ns)<sup>132</sup>
      - $12.8 \pm 4.4$  versus  $15.2 \pm 5.5$ , respectively ( $P = .045$ )<sup>136</sup>
      - $4.9 \pm 7.1$  versus  $13.0 \pm 10.1$ , respectively ( $P = .000$ )<sup>176</sup>
    - percent of patients achieving meaningful functional improvement: *there was no benefit:*
      - 40% or more: 91% versus 83%, respectively (ns)<sup>132</sup>
      - 50% or more: 83% versus 69%, respectively (ns)<sup>136</sup>
  - *Opioid use: there was no benefit* in either of the two studies<sup>132, 136</sup> reporting this outcome at twelve months:
    - $27.2 \pm 20.8$  versus  $28.6 \pm 15.6$ , respectively (ns)<sup>132</sup>

- $35 \pm 35.6$  versus  $33 \pm 10.9$ , respectively (ns)<sup>136</sup>
- *Employment: there was no difference* in the percent of eligible patients who were employed either part- or full-time in either of the two studies<sup>132, 136</sup> reporting this outcome at twelve months:
  - 94% versus 83%, respectively ( $P = \text{NR}$ )<sup>132</sup>
  - 88% versus 83%, respectively ( $P = \text{NR}$ )<sup>136</sup>

**Table 5. Pain and function outcomes from placebo-controlled trials of lumbar caudal or interlaminar epidural steroid injections for low back pain with sciatica or radiculopathy**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 1291 (17 studies)	NR	Interlaminar (13/17 studies) Caudal (4/17 studies)	NR	Positive (7/17 studies) Negative (7/17 studies) Unclear (p-value NR) (3/17 studies)		Positive (1/9 studies) Negative (7/9 studies) Mixed (1/9 studies) (NR: 8 studies)	
Manchikanti (2008, pt 2) <sup>132</sup>	RCT  LoE IIb	N = 120	Yes	Caudal (n = 42)	Epidural saline/ local anesth. (n = 42)	Negative (3 mos.)	Negative (ODI) (3 mos.)	Negative (12 mos.)	Negative (ODI) (12 mos.)
Manchikanti (2010) <sup>136</sup> (Evaluation of the effectiveness...)	RCT  LoE IIb	N = 120	Yes	Interlaminar (n = 35)	Epidural saline/ local anesth. (n = 35)	Negative (3 mos.)	Negative (ODI) (3 mos.)	Negative (12 mos.) *	Mixed† (ODI) (12 mos.)
Sayegh (2009) <sup>176</sup>	RCT  LoE IIb	N = 183	No	Caudal (n = 93)	Epidural water/ local anesth. (n = 90)	NR	Positive‡ (ODI) (1 mo.)	NR	Positive‡ (ODI) (12 mos.)

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

\* Manchikanti (2010)<sup>136</sup>: At 6 months, statistically more patients in the treatment group achieved pain relief of 50% or more (compared with baseline) than did those in the control group; similarly, mean pain scores were statistically lower in the treatment group versus the control group at 6 months. However, there were no differences in either of these outcomes by 12 months.

† Manchikanti (2010)<sup>136</sup>: At 12 months, mean ODI scores of the treatment group were statistically better (lower) compared with those of the control group, however there were no differences between groups in terms of the percent of patients achieving functional improvement of 50% or more (versus baseline).

‡ Sayegh (2009)<sup>176</sup> reported mean ODI scores only.

### ***Low back pain without sciatica or radiculopathy***

RCTs ≤ 2008: Chou *et al* (2009)<sup>39, 40</sup> concluded that there was insufficient evidence based on negative pain and function outcomes from one small lower-quality trial comparing epidural steroid to intrathecal midazolam injections, however, no other details (including length of follow-up) were reported (Table 6). The overall quality of evidence was considered to be poor.

RCTs ≥ 2008: We identified two additional RCTs<sup>116, 118</sup> published after the APS systematic review. Both studies received a level of evidence (LoE) grade of IIb. Detailed demographic and outcome data are available in Appendix L.

Treatment (steroid) versus placebo (saline and/or local anesthetic) epidural injection:

- Short-term (≤ 3 months):
  - *Pain: there was no benefit* as reported by 100% of two studies<sup>116, 118</sup> at three months (Table 6):
    - mean NRS scores (0-10 cm):
      - $3.7 \pm 1.4$  versus  $3.7 \pm 1.2$ , respectively (ns)<sup>118</sup>
      - $3.4 \pm 1.1$  versus  $3.7 \pm 1.0$ , respectively (ns)<sup>116</sup>
    - percent of patients achieving pain relief of 50% or more:
      - 78% versus 78%, respectively (ns)<sup>118</sup>
      - 86% versus 80%, respectively (ns)<sup>116</sup>
  - *Function: there was no benefit* as reported by 100% of two studies<sup>116, 118</sup> at three months (Table 6):
    - mean ODI scores (0-50 scale):
      - $14.1 \pm 5.4$  versus  $13.8 \pm 4.8$ , respectively (ns)<sup>118</sup>
      - $13.9 \pm 4.8$  versus  $14.6 \pm 4.1$ , respectively (ns)<sup>116</sup>
    - percent of patients achieving functional improvement by:
      - 40% or more: 81% versus 81%, respectively (ns)<sup>118</sup>
      - 50% or more: 80% versus 83, respectively (ns)<sup>116</sup>
  - *Opioid use: there was no benefit* as reported by 100% of two studies<sup>116, 118</sup> at three months:
    - $34.7 \pm 22.8$  versus  $31.2 \pm 29.9$  mg (morphine equivalents), respectively (ns)<sup>118</sup>
    - $49 \pm 59.8$  versus  $39 \pm 29.3$ , respectively (ns)<sup>116</sup>
- Long-term (> 3 months):
  - *Pain: there was no benefit* as reported by 100% of two studies<sup>116, 118</sup> at 12 months (Table 6):
    - mean NRS scores (0-10 cm):
      - $3.9 \pm 1.6$  versus  $3.7 \pm 1.2$ , respectively (ns)<sup>118</sup>
      - $3.8 \pm 1.3$  versus  $3.9 \pm 1.2$ , respectively (ns)<sup>116</sup>
    - percent of patients achieving pain relief of 50% or more:
      - 72% versus 72%, respectively (ns)<sup>118</sup>
      - 80% versus 80%, respectively (ns)<sup>116</sup>
  - *Length of pain relief: there was no benefit* as reported by 100% of two studies<sup>116, 118</sup> at 12 months:
    - $30.7 \pm 17.9$  weeks versus  $32.3 \pm 16.9$  weeks, respectively ( $P = \text{NR}$ )<sup>118</sup>
    - $33.9 \pm 16.0$  weeks versus  $37.4 \pm 14.7$  weeks, respectively ( $P = \text{NR}$ )<sup>116</sup>
  - *Function: there was no benefit* as reported by 100% of two studies<sup>116, 118</sup> at 12 months (Table 6):
    - mean ODI scores (0-50 scale):

- $13.8 \pm 5.3$  versus  $13.1 \pm 4.9$ , respectively (ns)<sup>118</sup>
- $15.9 \pm 6.9$  versus  $15.0 \pm 5.2$ , respectively (ns)<sup>116</sup>
- percent of patients achieving functional improvement by:
  - 40% or more: 81% versus 81%, respectively (ns)<sup>118</sup>
  - 50% or more: 60% versus 71%, respectively (ns)<sup>116</sup>
- *Opioid use: there was no benefit* as reported by 100% of two studies<sup>116, 118</sup> at 12 months:
  - $35.3 \pm 22.6$  versus  $30.9 \pm 30.1$  mg (morphine equivalents), respectively (ns)<sup>118</sup>
  - $42 \pm 44.2$  versus  $41 \pm 32.9$ mg (morphine equivalents), respectively (ns)<sup>116</sup>
- *Employment: results were unclear* in the percentage of eligible patients employed either part- or full-time at 12 months:
  - *there was no benefit* in one study<sup>118</sup>: 85% versus 82% , respectively ( $P = \text{NR}$ )
  - *results were unclear* in the other study<sup>116</sup>: (p-value not reported) but were higher in the epidural steroid injection group: 83% versus 64%, respectively ( $P = \text{NR}$ )

**Table 6. Pain and function outcomes from placebo-controlled trials of caudal or interlaminar epidural steroid injections for low back pain without radiculopathy**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	NR	NR	NR	Intra-thecal midazolam (n = NR)	Negative (length of f/u NR)			
Manchikanti (2008, pt 1) <sup>118</sup>	RCT  LoE IIb	N = 120	Yes	Caudal (n = 36)	Epidural saline/ local anesth. (n = 36)	Negative (3 mos.)	Negative (ODI) (3 mos.)	Negative (12 mos.)	Negative (ODI) (12 mos.)
Manchikanti (2010) <sup>116</sup> (Preliminary results of...)	RCT  LoE IIb	N = 120	Yes	Interlaminar (n = 35)	Epidural saline/ local anesth. (n = 35)	Negative (3 mos.)	Negative (ODI) (3 mos.)	Negative (12 mos.)	Negative (ODI) (12 mos.)

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

**Spinal stenosis**

RCTs/SRs ≤ 2008: Chou *et al* (2009)<sup>39, 40</sup> concluded that there was insufficient evidence with no clear benefit based on negative outcomes from three small trials comparing epidural steroid placebo injections (Table 7). One small study reported that patients in the epidural steroid group had improvements in walking distance at one week compared to patients in the placebo (epidural) group, however this benefit was not sustained and there were no differences between groups at three months. The other two studies conducted subgroup analyses on patients with spinal stenosis and found no differences in any reported outcomes between treatment groups in the short- or long-term (13-30 months). One of the studies was higher-quality, and two were lower-quality. No systematic reviews were noted. The overall quality of evidence was considered to be poor.

RCTs ≥ 2008: We identified one additional RCT<sup>115</sup> published after the APS systematic review; the study was given a LoE grade of IIb. Detailed demographic and outcome data are available in Appendix L.

Treatment (steroid) versus placebo (saline and/or local anesthetic) epidural injection:

- Short-term (≤ 3 months)
  - *Pain: there was no benefit* at three months (Table 7):
    - mean NRS scores (0-10 cm):  $4.2 \pm 2.4$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 50% versus 65%, respectively (ns)
  - *Function: there was no benefit* at three months (Table 7):
    - mean ODI scores (0-50 scale):  $16.4 \pm 8.3$  versus  $16.4 \pm 7.5$ , respectively (ns)
    - percent of patients achieving functional improvement by 40% or more: 50% versus 65%, respectively (ns)
  - *Opioid use: there was no benefit* three months:
    - $21.2 \pm 18.9$  versus  $35.6 \pm 53.1$  mg (morphine equivalents/day), respectively (ns)
- Long-term (> 3 months) – data excluded (> 20% of data in one of the groups were carried forward from the last available follow-up)

**Table 7. Pain and function outcomes from placebo-controlled trials of caudal or interlaminar epidural steroid injections for spinal stenosis**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 189 (3 studies)	NR	Interlaminar (2/3) Caudal (1/3)	Saline or saline/ anesth.	Negative (2/2) (NR: 1 study)		Negative (2/2) (NR: 1 study)	
Manchikanti (2008, pt 4) <sup>115</sup>	RCT  LoE IIb	N = 61	Yes	Caudal (n = 20)	Epidural saline/ local anesth. (n = 20)	Negative (3 mos.)	Negative (3 mos.) (ODI)	Data excluded*	Data excluded*

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

\* Data excluded for any follow-up in which < 20% of the data in either group were carried forward from the last available data point (applies to Manchikanti's studies only).

### ***Failed back surgery syndrome***

**RCTs/SRs ≤ 2008:** *Chou et al (2009)<sup>39, 40</sup> concluded that there was insufficient evidence with no clear benefit based on data from two small lower-quality placebo-controlled trials, however, no details (including length of follow-up) were reported (Table 8). No systematic reviews were noted. The overall quality of evidence was considered to be poor.*

**RCTs ≥ 2008:** We identified one additional RCT<sup>133</sup> (LoE IIb) published after the APS systematic review. Detailed demographic and outcome data are available in Appendix L.

Treatment (steroid) versus placebo (saline and/or local anesthetic) epidural injection:

- Short-term (≤ 3 months)
  - *Pain: there was no benefit* at three months (Table 8):
    - mean NRS scores (0 to 10 cm scale):  $4.1 \pm 1.5$  versus  $3.8 \pm 1.7$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 65% versus 70%, respectively (ns)
  - *Function: there was no benefit* at three months (Table 8):
    - mean ODI scores (0-50 scale):  $27.4 \pm 5.1$  versus  $28.9 \pm 5.2$ , respectively (ns)
    - percent of patients achieving functional improvement by 40% or more: 70% versus 70%, respectively (ns)
  - *Opioid use: there was no benefit* at three months:
    - $40.4 \pm 38.3$  versus  $32.5 \pm 22.3$  mg (morphine equivalents), respectively (ns)
- Long-term (> 3 months) – data excluded (> 20% of data in one of the groups were carried forward from the last available follow-up)

**Table 8. Pain and function outcomes from placebo-controlled trials of caudal or interlaminar epidural steroid injections for failed back surgery syndrome**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 228 (2 studies)	NR	NR	analgesic	Negative (2/2) (length of f/u NR)			
Manchikanti (2008, pt 3) <sup>133</sup>	RCT  LoE IIb	N = 68	Yes	Caudal (n = 20)	Epidural saline/ local anesth. (n = 20)	Negative (3 mos.)	Negative (3 mos.) (ODI)	Data excluded*	Data excluded*

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

\* Data excluded for any follow-up in which < 20% of the data in either group were carried forward from the last available data point (applies to Manchikanti's studies only).

#### 4.1.2. Lumbar transforaminal epidural injections versus placebo controls

RCTs/SRs ≤ 2008: *Chou et al (2009)<sup>39, 40</sup> concluded that there was mixed evidence* following transforaminal epidural injections for low back pain with sciatica based on data from three higher-quality studies. *Two of three studies showing no benefit* on most outcomes, however, we omitted data from one<sup>153</sup> in Table 9 since we identified a more recent continuation of this study (Tafazal (2009)<sup>197</sup> see below). Of the other two studies, only one reported short-term (≤ 3 months) data, and the results were mixed. More specifically, data suggested that transforaminal injection of steroid resulted in statistically better leg pain VAS scores at two weeks compared with injection of local anesthetic. However, the results were no longer meaningful at one and three months. There were no differences between treatment groups in the short-term in terms of back pain, function (ODI and Nottingham), and sick leave days. Long-term (> 3 months) data were available in both the studies, with one reporting positive and the other reporting negative results. No systematic reviews were noted. The overall quality of evidence was considered to be fair.

RCTs ≥ 2008: We identified two RCTs. One RCT<sup>64</sup> compared transforaminal injections of steroids/local anesthetic to those with local anesthetic or saline (there were also two intramuscular injection control groups; these are summarized in section 4.1.3). The second RCT<sup>197</sup> appeared to be a continuation of one<sup>153</sup> of the three studies that was included in the Chou et al (2009) systematic review<sup>39, 40</sup>. In comparison with the study reported in Chou, this updated version included an additional 72 patients (for a total of 150 patients); the enrollment period was extended by two years. All data summarized in the Chou SR<sup>39</sup> appear to be included in this report. The study received a level of evidence grade of IIb. Detailed demographic and outcome data are available in Appendix L.

Treatment (steroid) versus placebo (local anesthetic<sup>64, 197</sup> versus saline<sup>64</sup>) epidural injection:

- Short-term (≤ 3 months)
    - *Pain:* results were mixed as reported by two studies<sup>64, 197</sup>, with a benefit at one month in one study<sup>64</sup> and no benefit at three months in the other study<sup>197</sup> (Table 9):
      - one month: percent of patients achieving pain relief of 50% or more: 54% (95% CI, 36%, 72%) versus 7% (95% CI, 0%, 17%) versus 19% (95% CI, 6%, 32%), respectively ( $P = \text{NR}$ )<sup>64</sup>
      - one month: mean ± SD VAS leg pain scores (0-100 mm):  $4.1 \pm 3.0$  versus  $6.7 \pm 2.8$  ( $P = .002$ ) versus  $5.5 \pm 2.6$  (ns)<sup>64</sup>
      - three months: percent change in VAS leg or back pain scores (0-100 mm):  $24.5 \pm 3.6$  versus  $22.6 \pm 4.1$ , respectively (ns)<sup>197</sup>
    - *Function:* *there was no benefit* at three months (12 weeks) as reported by one study<sup>197</sup> (Table 9):
      - percent change in ODI (0-100 scale):  $9.3 \pm 2.3$  versus  $10.7 \pm 2.6$ , respectively (ns)
      - percent change in LBOS (0-75 scale):  $9.1 \pm 2.0$  versus  $9.4 \pm 2.3$ , respectively (ns)
- In the other RCT<sup>64</sup>, mean function (Roland-Morris) (and SF-36 quality of life) scores were not reported for each treatment group. The authors reported the median scores for successful versus unsuccessful patients. In most cases, “successful” (pain relief ≥ 50%) patients had statistically better function and quality of life compared with their “unsuccessful” counterparts, suggesting that pain relief of at least 50% typically corresponds with improvements in function and quality of life. Detailed scores may be found in Appendix L.
- Long-term (> 3 months)
    - *Additional interventions:* *there was no benefit* up to 12 months as reported by two studies<sup>64, 197</sup> in terms of the percent of patients who required:

- surgery:
  - 14.1% versus 21.5%, respectively (ns) (12 months)<sup>197</sup>
  - 36% (10/28) versus 26% (7/27) versus 27% (10/37) ( $\leq 12$  months; surgery was offered if patients felt they didn't have adequate relief)<sup>64</sup>
- transforaminal (peri-radicular) injections (12 months): 12.5% versus 15.4%, respectively (ns)
- The remaining long-term data from one study<sup>64</sup> were difficult to interpret due to follow up rates less than 25%: patients were followed only until they registered their allocated treatment as a failure; as a result, follow-up at three months was 23% (34/150) and further declined through twelve months. Of the patients who reported treatment success at one month, there was no benefit in terms of the median length of pain relief following transforaminal steroid injections versus local anesthetic or saline injections (details can be found in Appendix L).

**Table 9. Pain and function outcomes from placebo-controlled trials of transforaminal epidural steroid injections for low back pain with radiculopathy**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 215* (2* studies)	NR	Transforaminal	NR	Positive (0/1) Mixed (1/1)† (NR: 1 study)		Positive (1/2) Negative (1/2)	
Ghahreman (2010) <sup>64</sup>	RCT  LoE IIb	N = 150	Yes	Transforaminal (n = 28)	Transforaminal (local anesth.) (n = 27) ;  Transforaminal (saline) (n = 37)	Positive (1 mos.) (pain relief ≥ 50%)	Unable to evaluate‡	§	§
Tafazal* (2009) <sup>197</sup>	RCT  LoE IIb	N = 150*	Yes	Transforaminal (peri-radicular) (n = 74)	Transforaminal (local anesth.) (n = 76)	Negative (3 mos.)	Negative (ODI, LBOS) (3 mos.)	NR	NR

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

\* Chou (2009) included data on three studies, one of which was omitted in our review of the evidence included in this systematic review as a continuation of this study (Ng (2005)<sup>153</sup>) was published in 2009 and is included here (Tafazal (2009)<sup>197</sup>).

† Chou (2009): Mixed short-term data: positive leg pain relief at two weeks but negative at four weeks and three months; negative back pain relief ≤ 3 months; negative function (ODI and Nottingham) ≤ 3 months.

‡ Ghahreman (2010) We were unable to determine the results. The authors did not report the mean or median one-month Roland-Morris scores, SF-36, or leg pain VAS scores for each treatment group. Instead, they reported the median scores for two subgroups (successful versus unsuccessful patients) in each treatment group. Because these scores were reported as the median (instead of the mean), we were unable to calculate the median or mean outcome scores for each treatment group at one month follow-up.

§ Ghahreman (2010) only followed all patients (regardless of outcome) until one month. After this point, patients could register as having failed a treatment once they no longer had pain relief and wanted to obtain a different treatment; as a result of this study methodology, follow-up after one month was ≤ 23% and therefore data were difficult to interpret (see Appendix L).

#### 4.1.3. Lumbar epidural steroid injections versus non-placebo controls

RCTs/SRs ≤ 2008: *Chou et al (2009)*<sup>39, 40</sup> (no systematic reviews were reported)

Efficacy of lumbar epidural steroid injections (Table 10):

- versus trigger point injections: *epidural steroid injections were “modestly superior”* to trigger point injections at three months in patients with sciatica and radiculopathy in data from one higher-quality study; there were no differences between treatment groups at one month. The overall quality of evidence was considered to be fair.
- versus dry needling of the interspinous ligament: *there was insufficient evidence* to assess the efficacy of epidural steroids compared with dry needling of the interspinous ligament, with one lower-quality study reporting no benefit in patients with sciatica. The overall quality of evidence was considered to be poor.
- versus intramuscular steroid injections: *there was no benefit* of epidural steroid injection compared with intramuscular steroid injections according to data from one small higher-quality trial in terms of pain relief or the need for subsequent surgery at two years in patients with low back pain with sciatica. The overall quality of evidence was considered to be fair.
- versus discectomy: *epidural steroid injections were inferior* to discectomy in the short-term in patients with lumbar disc prolapse according to data from one higher quality trial. Long-term data (2-3 years) suggested that there were no differences between the treatments, however, these results were less clear due to high rates of cross-over. The overall quality of evidence was considered to be poor.
- versus transforaminal oxygen-ozone injections: *there was no benefit* of transforaminal (and/or intradiscal) epidural injections of steroid alone compared with steroid plus oxygen-ozone in the short-term; injections of steroid alone were inferior to those of steroids plus oxygen-ozone in the long-term (6 months). Data were reported by two lower-quality studies evaluating patients with low back pain and sciatica; the overall quality of evidence was considered to be poor.
- versus adhesiolysis: *there was no benefit* of epidural steroid injections compared with adhesiolysis (with saline ± steroid OR hyaluronic acid) at four months to one year as reported by three studies, one of which was higher-quality study. The two lower-quality studies evaluated patients with failed back surgery syndrome; while the higher-quality study enrolled patients who had not responded to a prior epidural steroid injection for treatment of chronic back pain (> 2 years duration), thus this study compared a treatment known to be ineffective in the patients being treated to adhesiolysis. The overall quality of evidence was considered to be poor.

RCTs ≥ 2008: Four additional studies<sup>64, 99, 117, 134</sup> were identified that compared lumbar epidural steroid injections to non-placebo controls. Detailed demographic and outcome data are available in Appendix L.

versus adhesiolysis: two RCTs<sup>117, 134</sup>, both of which receive LoE grades of IIb, evaluated outcomes following caudal epidural versus epidural percutaneous adhesiolysis injections with steroids, saline, and local anesthetic. For these two studies, patients treated with epidural steroids formed the control group, while those who received adhesiolysis consisted of the treatment group. Patients were treated for low back pain due to spinal stenosis and radiculitis in one study<sup>117</sup> and for failed back surgery syndrome (FBSS) in the other<sup>134</sup>; due to these different diagnoses, results were not pooled. Of note, in order to meet the inclusion criteria in both these studies, patients must have failed to respond to a prior fluoroscopically-guided epidural steroid injection, therefore these studies compared a treatment known to be ineffective in the patients being

treated to adhesiolysis. Thus, the outcomes of these studies could have been predicted to favor adhesiolysis due to the study design alone.

Treatment (steroid) versus active control (adhesiolysis):

- Short-term ( $\leq 3$  months)
  - *Pain: there was no benefit* (inferior results) in patients who had failed prior epidural steroid injections in either study<sup>117, 134</sup> at three months (Table 10):
    - mean NRS scores (0-10 cm):
      - stenosis/radiculitis:  $5.4 \pm 1.6$  versus  $3.6 \pm 1.2$ , respectively ( $P = .000$ )
      - FBSS:  $4.9 \pm 1.6$  versus  $3.4 \pm 0.8$ , respectively ( $P = .000$ )
    - percent of patients achieving pain relief of 50% or more:
      - stenosis/radiculitis: 28% versus 80%, respectively ( $P = \text{NR}$ )
      - FBSS: 35% versus 90%, respectively ( $P < .05$ )
  - *Function: there was no benefit* (inferior results) in patients who had failed prior epidural steroid injections in either study<sup>117, 134</sup> at three months (Table 10):
    - mean ODI scores (0-50 scale):
      - stenosis/radiculitis:  $23.3 \pm 6.2$  versus  $15.6 \pm 5.3$ , respectively ( $P = .000$ )
      - FBSS:  $20.2 \pm 6.6$  versus  $15.2 \pm 4.1$ , respectively ( $P = .000$ )
    - percent of patients achieving functional improvement of 40% or more:
      - stenosis/radiculitis: 24% versus 80%, respectively ( $P = \text{NR}$ )
      - FBSS: 37% versus 92%, respectively ( $P = \text{NR}$ )
  - *Opioid use: there was no benefit* (inferior results) in patients who had failed prior epidural steroid injections in either study<sup>117, 134</sup> at three months (Table 10):
    - stenosis/radiculitis:  $35.5 \pm 12.4$  versus  $32 \pm 13.8$  mg (morphine equivalents), respectively (ns)
    - FBSS:  $42 \pm 28.6$  versus  $42 \pm 28.9$  mg (morphine equivalents), respectively (ns)
- Long-term ( $> 3$  months) – data excluded ( $> 20\%$  of data in one of the groups were carried forward from the last available follow-up).

**versus physical therapy/control:** one RCT<sup>99</sup> (LoE IIb) compared patients receiving interlaminar epidural steroid injections ( $n = 10$ ) with those treated with physical therapy alone ( $n = 10$ ) and control patients (no treatment details reported;  $n = 9$ ). All patients had been diagnosed with spinal stenosis.

Treatment (steroid) versus physical therapy versus control group:

- Short-term ( $\leq 3$  months):
  - *Pain: there was no benefit* at three months (Table 10):
    - mean VAS scores (0-100 mm): 23 versus 24 versus 38, respectively (ns between tx and PT or control)
    - VAS subscale Nottingham Health Profile scores (median percent change): 20.5% versus 18.2% versus 27.7%, respectively (ns between tx and PT or control)
  - *Function: there was no benefit* in function at three months (Table 10):
    - mean Roland-Morris Disability Index (RMDI) scores (0-24 scale): 11 versus 11 versus 10, respectively (ns between tx and PT or control)
    - physical mobility Nottingham Health Profile subscale scores (median percent change): 31.2% versus 32.5% versus 31.0%, respectively (ns between tx and PT or control)

- *Quality of life: there was no benefit* at three months in the median percent change of the following Nottingham Health Profile subscale scores:
  - energy: 62.0% versus 30.4% versus 100%, respectively (ns between tx and PT or control)
  - sleep: 14.3% versus 12.5% versus 28.6%, respectively (ns between tx and PT or control)
  - social isolation: 32.0% versus 11.0% versus 0%, respectively (ns between tx and PT or control)
  - emotional reactions: 41.4% versus 0% versus 9.7%, respectively (ns between tx and PT or control)
- Long-term (> 3 months):
  - *Pain: there was no benefit* at six months (Table 10):
    - mean VAS scores (0-100 mm): 26 versus 22 versus 33, respectively (ns between tx and PT or control)
    - VAS subscale Nottingham Health Profile scores (median percent change): 23.0 versus 23.2 versus 20.1, respectively (ns between tx and PT or control)
  - *Function: there was no benefit* in function at six months (Table 10):
    - mean Roland-Morris Disability Index (RMDI) scores (0-24 scale): 13 versus 12 versus 9, respectively (ns between tx and PT or control)
    - physical mobility Nottingham Health Profile subscale scores (median percent change): 31.2% versus 37.1% versus 20.5%, respectively (ns between tx and PT or control)
  - *Quality of life: there was no benefit* at six months in the median percent change of the following Nottingham Health Profile subscale scores:
    - energy: 81.6% versus 48.8% versus 63.2%, respectively (ns between tx and PT or control)
    - sleep: 25.5% versus 12.5% versus 12.5%, respectively (ns between tx and PT or control)
    - social isolation: 32.3% versus 0% versus 0%, respectively (ns between tx and PT or control)
    - emotional reactions: 27.5% versus 6.9% versus 0%, respectively (ns between tx and PT or control)

**versus intramuscular injection (local anesthetic or saline):** One RCT<sup>64</sup> compared transforaminal injections of steroids to intramuscular injections with local anesthetic or saline (there were also two placebo injection control groups; these are summarized in section 4.1.2).

Treatment (transforaminal injection of steroid) versus intramuscular injection of local anesthetic or saline):

- Short-term ( $\leq 3$  months)
  - *Pain: there was no benefit* at one month for transforaminal steroid versus local anesthetic injections AND *results were mixed* at one month for transforaminal steroid versus saline injections (Table 10):
    - one month: percent of patients achieving pain relief of 50% or more: 54% (95% CI, 36%, 72%) versus 21% (95% CI, 6%, 36%) versus 13% (95% CI, 1%, 25%), respectively ( $P = \text{NR}$ )<sup>64</sup>
    - one month: mean  $\pm$  SD VAS leg pain scores (0-100 mm):  $4.1 \pm 3.0$  versus  $6.7 \pm 2.8$  ( $P = .002$ ) versus  $5.5 \pm 2.6$  (ns)<sup>64</sup>

- *Function:* Mean function (Roland-Morris) (and SF-36 quality of life) scores were not reported for each treatment group. The authors reported the median scores for successful versus unsuccessful patients. In most cases, “successful” (pain relief  $\geq 50\%$ ) patients had statistically better function and quality of life compared with their “unsuccessful” counterparts, suggesting that pain relief of at least 50% typically corresponds with improvements in function and quality of life. Detailed scores may be found in Appendix L.
- Long-term (> 3 months)
  - *Surgery:* *there was no benefit* in terms of the percent of patients who underwent surgery (which was offered if patients felt they didn’t have adequate relief): 36% (10/28) versus 21% (6/28) versus 30% (9/30)
  - The remaining long-term data<sup>64</sup> were difficult to interpret due to follow up rates less than 25%: patients were followed only until they registered their allocated treatment as a failure; as a result, follow-up at three months was 23% (34/150) and further declined through twelve months. Of the patients who reported treatment success at one month, there was no benefit in terms of the median length of pain relief following transforaminal steroid injections versus intramuscular injections of local anesthetic or saline (details can be found in Appendix L).

**Table 10. Pain and function outcomes from trials comparing lumbar epidural steroid injections to non-placebo controls**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	NR (1 study)	NR	NR	Trigger point injection	Positive (1/1)		NR	
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 74 (1 study)	NR	NR	Dry needling: inter-spinous ligament	Negative (length of f/u NR)			
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 92 (1 study)	NR	Interlaminar (n = 44)	Intra-muscular steroid injection (n = 48)	NR		Negative (1/1)	
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 100 (1 study)	NR	NR	Disc-ectomy	Negative (1/1)		Negative (1/1)	
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 100 (2 studies)	NR	Transforaminal (and intradiscal in one study)	Transforaminal (± intra-discal) oxygen-ozone/steroid	Negative (2/2)		Negative (2/2)	
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 182 (3 studies)	NR	NR	Adhesiolysis (saline ± steroid or hyaluronidase)	NR		Negative (3/3)	
Manchikanti (2009) <sup>117</sup> (The preliminary results...)	RCT  LoE IIb	N = 82 spinal stenosis	Yes	Caudal (n = 25)	Percutaneous epidural adhesiolysis (steroid/saline/local anesth.)	Negative (3 months)	Negative (ODI) (3 months)	Data excluded*	Data excluded*
Manchikanti (2009) <sup>134</sup> (A comparative effectiveness...)	RCT  LoE IIb	N = 180 failed back surgery synd.	Yes	Caudal (n = 60)	Percutaneous epidural adhesiolysis (steroid/saline/local anesth.)	Negative (3 months)	Negative (ODI) (3 months)	Data excluded*	Data excluded*
Koc (2009) <sup>99</sup>	RCT  LoE IIb	N = 33 spinal stenosis	Yes	Interlaminar (n = 10)	Physical therapy (PT) (n = 10) OR control† (n = 9)	Negative (both PT and control) (3 months)	Negative (both PT and control) (3 months)	Negative (both PT and control) (6 months)	Negative (both PT and control) (6 months)
Ghahreman	RCT	N = 150	Yes	Transforam-	Intra-	Positive	Unable to	§	§

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
(2010) <sup>64</sup>	LoE IIb			inal (n = 28)	muscular (local anesth.) (n = 28) ;  Transfor- aminal (saline) (n = 30)	(1 mos.) (pain relief ≥ 50%)	evaluate†‡		

NR: not reported

PT: physical therapy

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

\* Data excluded for any follow-up in which < 20% of the data in either group were carried forward from the last available data point (applies to Manchikanti's studies only).

† Koc (2009): no description of the treatment received was provided for the control group.

‡ Ghahreman (2010) We were unable to determine the results. The authors did not report the mean or median one-month Roland-Morris scores, SF-36, or leg pain VAS scores for each treatment group. Instead, they reported the median scores for two subgroups (successful versus unsuccessful patients) in each treatment group. Because these scores were reported as the median (instead of the mean), we were unable to calculate the median or mean outcome scores for each treatment group at one month follow-up.

§ Ghahreman (2010) only followed all patients (regardless of outcome) until one month. After this point, patients could register as having failed a treatment once they no longer had pain relief and wanted to obtain a different treatment; as a result of this study methodology, follow-up after one month was ≤ 23% and therefore data were difficult to interpret (see Appendix L).

## **SUMMARY: Efficacy of lumbar epidural steroid injections:**

- For trials comparing lumbar caudal or interlaminar epidural steroid with placebo injections for the treatment of:
  - low back pain with sciatica or radiculopathy, there is mixed evidence for both the short- ( $\leq 3$  months) and long- ( $> 3$  months) term based on data from up to 20 RCTs (7 of which were higher-quality) (strength of evidence = low).
  - low back pain without sciatica or radiculopathy, there is no benefit based on evidence from three lower-quality RCTs (strength of evidence = moderate).
  - spinal stenosis, there is no benefit based on evidence from four RCTs, one of which was higher-quality (strength of evidence = low to moderate).
  - failed back surgery syndrome, there is no benefit based on evidence from three lower-quality RCTs (strength of evidence = moderate).
  
- For trials comparing lumbar caudal or interlaminar epidural steroid injections with:
  - adhesiolysis, there is no benefit based on data from five RCTs, four of which were lower-quality (strength of evidence = low).
  - physical therapy for spinal stenosis, there is no benefit based on data from one lower-quality RCT (strength of evidence = very low).
  - trigger point injection therapy for sciatica and radiculopathy, there is evidence that epidural steroid injections were modestly superior based on data from one higher-quality RCT (strength of evidence = low).
  - dry needling of the interspinous ligament for sciatica, there is no benefit based on data from one lower-quality RCT (strength of evidence = very low).
  - intramuscular steroid injections for low back pain with sciatica, there is no benefit based on data from one higher-quality RCT (strength of evidence = low).
  - discectomy for disc prolapse, there is no benefit based on data from one higher-quality RCT (strength of evidence = low).
  
- For trials comparing lumbar transforaminal epidural steroid injections with:
  - placebo injections for low back pain with sciatica or radiculopathy, there is mixed evidence based on data from four RCTs, two of which were higher-quality (strength of evidence = low). In terms of pain relief, the data suggest a benefit at two weeks (one study), mixed results at one month (two studies- one positive and one negative), and no benefit by 3 months. No benefit in function was reported at three months by two studies. Long-term data were mixed as reported by two higher-quality RCTs, with one study reported positive results while the other showed no benefit.
  - intramuscular injections with local anesthetic or saline, there is evidence that transforaminal steroid injections were superior to intramuscular injections in terms of pain relief at one month based on data from one LoE IIb RCT (strength of evidence = low).
  - oxygen-ozone  $\pm$  steroids for disc prolapse, there is no benefit based on data from two lower-quality RCTs (strength of evidence = low).

#### 4.1.4. Lumbar facet interventions versus placebo (saline and/or local anesthetic) controls

##### *Intraarticular facet joint injections versus placebo controls*

RCTs/SRs ≤ 2008: Chou *et al* (2009)<sup>39, 40</sup> concluded that there was no benefit associated with facet joint injections with steroids versus saline (control) in patients with presumed facet joint pain based on data from two trials (Table 11). One study was higher-quality, and evaluated patients who had responded to a diagnostic facet joint injection of local anesthetic; the other study was lower-quality, and did not require a positive response to the diagnostic block. While the higher-quality study reported statistically meaningful benefits following facet steroid injections in some pain outcomes at six months, the results had not been significant at three months and Chou questioned the biologic rationale for the delayed response. Of note, the group that received the injection received more co-interventions (physical therapy), and the differences were attenuated after controlling for this. In addition, there was no difference in the proportion of patients with *sustained* pain relief at three and six months.

Four systematic reviews<sup>21, 166, 182, 190</sup> evaluated the efficacy of facet joint steroid compared with placebo injections. One higher-quality Cochrane review<sup>190</sup> and two lower-quality systematic reviews<sup>166, 182</sup> reported no benefit associated with facet joint steroid injections, while one lower-quality systematic review<sup>21</sup> reported moderate evidence that there was a short-term benefit following facet joint steroid injections.

The overall quality of evidence was considered to be fair.

RCTs ≥ 2008: No additional studies were identified.

**Table 11. Pain and function outcomes from placebo-controlled trials of lumbar intraarticular facet joint injections**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Diagnostic block?	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 210 (2 studies)	NR	Yes (1/2) No (1/2)	Facet injection with saline (n = NR)	Negative (2/2)		Mixed (1/1)	

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

### ***Therapeutic medial branch blocks versus placebo controls***

RCTs/SRs ≤ 2008: Chou et al (2009)<sup>39, 40</sup> did not identified any studies.

RCTs ≥ 2008: We identified one RCT<sup>135</sup> (LoE IIb) published after the Chou et al (2009) systematic review<sup>39</sup>. Detailed demographic and outcome data are available in Appendix M.

Treatment (steroid) versus placebo (local anesthetic) injection:

- Short-term (≤ 3 months)
  - *Pain: there was no benefit* at three months (Table 12):
    - mean NRS scores (0-10 cm):  $3.5 \pm 1.1$  versus  $3.8 \pm 1.3$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 82% versus 83%, respectively (ns)
  - *Function: there was no benefit* at three months (Table 12):
    - mean ODI scores (0-50 scale):  $13.5 \pm 5.6$  versus  $12.7 \pm 4.7$ , respectively ( $P = \text{NR}$ )
    - percent of patients achieving functional improvement of 40% or more: 72% versus 82%, respectively ( $P = \text{NR}$ )
- Long-term (> 3 months)
  - *Pain: there was no benefit* at 24 months (Table 12):
    - mean NRS scores (0-10 cm):  $3.2 \pm 0.9$  versus  $3.5 \pm 1.5$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 90% versus 85% (ns)
  - *Length of pain relief: there was no benefit* in the mean length of pain relief:  $84 \pm 27.5$  versus  $82 \pm 31.8$  weeks, respectively ( $P = \text{NR}$ ).
  - *Function: there was no benefit* at 24 months (Table 12):
    - mean ODI scores (0-50 scale):  $11.0 \pm 4.8$  versus  $12.0 \pm 4.9$ , respectively ( $P = \text{NR}$ )
    - percent of patients achieving functional improvement of 40% or more: 88% versus 87%, respectively ( $P = \text{NR}$ )
  - *Opioid use: there was no benefit* at (12 or) 24 months in the mean daily morphine equivalents used by either treatment group:  $30.0 \pm 27.1$  versus  $27.0 \pm 23.8$  mg, respectively (ns).

**Table 12. Pain and function outcomes from placebo-controlled trials of lumbar therapeutic medial branch blocks**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Diagnostic block?	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Manchikanti (2010) <sup>135</sup> (Evaluation of lumbar...)	RCT  LoE IIb	N = 120	Yes	Yes	Local anesth. injection (n = 42)	Negative (3 months)	Negative (3 months)	Negative (24 months)	Negative (24 months)

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

### **4.1.5 Lumbar facet interventions versus non-placebo controls**

RCTs/SRs ≤ 2008: Chou et al (2009)<sup>39, 40</sup> (no systematic reviews were reported)

Efficacy of lumbar facet steroid injections/ medial branch block (Table 13):

- versus home stretching: *there was no benefit in facet joint steroid injections plus home stretching* versus home stretching alone in patients with “presumed” lumbar segmental rigidity

according to data from one lower-quality study. The follow-up was not reported. The overall quality of evidence was considered to be poor.

- versus facet joint injections with hyaluronic acid: *there was no benefit in steroid* versus hyaluronic facet joint injections in patients with non-radicular back pain and moderate or greater facet joint osteoarthritis at six months according to data from one higher-quality study that was also included in one systematic review. The overall quality of evidence was considered to be fair.
- versus medial branch blocks with local anesthetic and/or Sarapin: *there was no benefit in medial branch blocks with steroid ( $\pm$  Sarapin)* versus local anesthetic  $\pm$  Sarapin in two trials. The outcomes measured were not reported; follow-up was not reported for the higher-quality study and ranged from 3-12 months in a lower-quality study. The overall quality of evidence was considered to be poor.

RCTs  $\geq$  2008: No additional studies were identified.

**Table 13. Pain and function outcomes from trials of lumbar intraarticular facet joint injections or medial branch blocks versus non-placebo controls**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Diagnostic block?	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = NR (1 study)	NR	NR	Home stretching	Negative (1/1) (follow-up NR)			
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 60 (1 study)	NR	No	Facet injection with hyaluronic acid	NR		Negative (1/1) (6 months)	
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 133 (2 studies)	NR	NR	Medial branch blocks with local anesth. ± Sarapain	Negative (2/2) (follow-up NR)			

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

**SUMMARY: Efficacy of lumbar facet joint interventions:**

- For trials comparing lumbar intraarticular facet joint steroid injections with:
  - placebo injections for confirmed or presumed facet joint pain, there is no benefit based on data from two RCTs, one of which was higher-quality (strength of evidence = low).
  - home stretching for presumed facet joint pain, there is no benefit based on data from one lower-quality RCT (strength of evidence = very low).
  - facet injections with hyaluronic acid for non-radicular back pain and facet joint osteoarthritis, there is no benefit based on data from one higher-quality RCT (strength of evidence = low).
- For trials comparing lumbar medial branch blocks with:
  - placebo injections for confirmed facet joint pain, there is no benefit based on data from one lower-quality RCT (strength of evidence = very low).
  - sarapin injections for presumed facet joint pain, there is no benefit based on data from two RCTs, one of which was higher-quality (strength of evidence = low).

#### 4.1.6 Sacroiliac joint injections versus placebo (saline and/or local anesthetic) controls

RCTs/SRs  $\leq$  2008: Chou *et al* (2009)<sup>39, 40</sup> concluded sacroiliac joint steroid injections were superior to placebo injections with local anesthetic alone at one month in patients with sacroiliac joint pain without spondyloarthropathy. Conclusions were based on data from one small higher-quality trial in which patients underwent a periarticular sacroiliac injection (Table 14). One higher-quality systematic review was also identified<sup>77</sup>, but its conclusions were not reported. The overall quality of evidence was considered to be poor.

RCTs  $\geq$  2008: No additional studies were identified.

**Table 14. Pain and function outcomes from trials of sacroiliac joint injections versus placebo controls**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Sacroiliac joint injection (n)	Control (n)	Short-term results ( $\leq$ 3 months)		Long-term results ( $>$ 3 months)	
						Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 24 (1 study)	NR	Peri-articular steroid injection (n = NR)	Local anesth. injection (n = NR)	Positive (1/1) (1 month)		NR	

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

#### **SUMMARY: Efficacy of sacroiliac joint steroid interventions:**

- For trials comparing sacroiliac joint steroid injections with:
  - placebo injections for sacroiliac joint pain, there is evidence that sacroiliac joint steroid injections were superior to placebo injections based on data from one higher-quality RCT (strength of evidence = low).

#### 4.1.7 Lumbar intradiscal injections versus placebo (saline and/or local anesthetic) controls

RCTs/SRs ≤ 2008: Chou et al (2009)<sup>39, 40</sup> found no benefit associated with intradiscal steroid injections versus those with saline or local anesthetic alone in patients with presumed discogenic low back pain based on data from one small higher-quality and one larger lower-quality trial (Table 15).

A third trial was also identified and compared intradiscal steroid injections with discography with discography alone in patients with degenerative disc disease. Again, no benefit was associated with intradiscal steroid injections except for in a subgroup of patients with inflammatory endplate changes on MRI, for whom intradiscal injections were superior (Table 15).

One higher-quality systematic review was also identified<sup>65, 66</sup>, but no conclusions were reported. The overall quality of evidence was considered to be good.

RCTs ≥ 2008: We identified one additional RCT<sup>161</sup> published after the Chou et al (2009) systematic review<sup>39</sup> which compared intradiscal injections with methylene blue/local anesthetic (n = 36) to those with saline/local anesthetic (n = 36). This study differs from the rest of the studies in this report in that it utilizes a neurolytic agent (methylene blue) instead of a steroid. Patients had low back pain (without radiculopathy) due to lumbar disc degeneration. The study received an LoE grade of IIa. Detailed demographic and outcome data are available in Appendix N.

Treatment (methylene blue) versus placebo (saline/local anesthetic) injection:

- Short-term (≤ 3 months): no data reported
- Long-term (> 3 months)
  - *Pain: intradiscal injections with methylene blue were superior* to placebo injections as reported at 6-24 months (Table 15):
    - mean NRS pain scores (24 months) (0-100 mm): 19.8 ± 16.0 versus 60.4 ± 14.1 ( $P < .001$ )
  - *Function: intradiscal injections with methylene blue were superior* to placebo injections at 6-24 months follow-up (Table 15):
    - mean ODI scores (24 months) (0-100 scale): 12.9 ± 12.0 versus 47.7 ± 10.9, respectively ( $P < .001$ )
  - *Patient satisfaction: intradiscal injections with methylene blue were superior* to placebo injections at 24 months in terms of the percent of patients who were :
    - completely satisfied: 19% versus 0%, respectively ( $P < .001$ )
    - satisfied: 72% versus 14%, respectively ( $P < .001$ )
    - unsatisfied: 8% versus 86%, respectively ( $P < .001$ )
  - *Medication usage: intradiscal injections with methylene blue were superior* to placebo injections at 24 months. The usage of nonsteroidal anti-inflammatory drugs or opioid medications was considered to be:
    - none: 83.3% versus 5.7%, respectively ( $P < .001$ )
    - occasional (term not defined): 8.3% versus 51.4%, respectively ( $P < .001$ )
    - regular (term not defined): 8.3% versus 42.9% ( $P < .001$ )

**Table 15. Pain and function outcomes from trials of lumbar intradiscal injections versus placebo controls**

Study	Study type/	Sample size (N)	Fluor. guidance?	Intra-discal	Control (n)	Short-term results (≤ 3 months)	Long-term results (> 3 months)
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	LoE			injection		Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = 316 (3 studies)	NR	Steroid (n = NR)	Injection with anesthes. or saline; or discography (n = NR)	Negative (1/1) (10-14 days)		Negative* (2/2) (1-2 years)	
Peng (2010) <sup>161</sup>	RCT  LoE IIa	N = 72	Yes	Methylene blue/ local anesthes. (n = 36)	Saline/ local anesthes. (n = 36)	NR	NR	Positive (1/1) (24 months)	Positive (1/1) (24 months)

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

\*except in a subgroup of patients with inflammatory endplate changes on MRI, for whom intradiscal steroid injections were superior at 1-2 years.

#### 4.1.8 Lumbar intradiscal injections versus non-placebo controls

RCTs/SRs ≤ 2008: Chou *et al* (2009)<sup>39, 40</sup> found no benefit associated with intradiscal steroid injections versus chemonucleolysis in sciatica patients according to data from three studies, one of which was higher-quality (Table 16). Two studies (in French) were included in a Cochrane review<sup>65, 66</sup>. The overall quality of evidence was considered to be good.

RCTs ≥ 2008: No additional studies were identified.

**Table 16. Pain and function outcomes from trials of lumbar intradiscal injections versus non-placebo controls**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
					Pain	Function	Pain	Function
Chou (2009) <sup>39, 40</sup> (APS SR)	SR	N = NR (3 studies)	NR	Chemo-nucleolysis (n = NR)	Negative (3/3) (follow-up NR)			

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

\*except in a subgroup of patients with inflammatory endplate changes on MRI, for whom intradiscal steroid injections were superior at 1-2 years.

#### **SUMMARY: Efficacy of lumbar intradiscal steroid interventions:**

- For trials comparing lumbar intradiscal steroid injections with:
  - placebo injections for discogenic back pain, there is no benefit based on data from three RCTs, one of which was higher-quality (strength of evidence = moderate).
  - chemonucleolysis for sciatica, there is no benefit based on data from three RCTs, one of which was higher-quality (strength of evidence = moderate).
- For trials comparing lumbar intradiscal injections using a neurolytic agent with:
  - placebo injections for low back pain without radiculopathy, there is evidence that intradiscal injections with methylene blue were superior to placebo injections based on data from one higher-quality RCT (strength of evidence = low).

## Cervical spinal injections

### 4.1.9 Cervical epidural injections versus placebo (saline and/or local anesthetic) controls

#### *Neck pain with disc herniation and radiculitis*

We identified one RCT (LoE IIb), which compared fluoroscopically guided cervical interlaminar epidural injections with local anesthetic in the presence (n = 35) or absence (n = 35) of steroids. Patients had chronic neck pain with disc herniation and radiculitis. Detailed demographic and outcome data are available in Appendix O.

Treatment (steroid) versus placebo (saline and/or local anesthetic) epidural injection:

- Short-term ( $\leq 3$  months):
  - *Pain: there was no benefit* associated with cervical epidural steroid injections (negative results) at three months (Table 17):
    - mean NRS scores (0-10 cm):  $3.4 \pm 1.1$  versus  $3.2 \pm 1.1$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 83% versus 89%, respectively (ns)
  - *Function: there was no benefit* at three months (Table 17):
    - mean NDI scores (0-50 scale):  $14.1 \pm 5.6$  versus  $14.6 \pm 5.7$ , respectively (ns)
    - percent of patients achieving functional improvement of 50% or more 77% versus 77%, respectively (ns)
  - *Opioid use: there was no benefit* at three months in the daily morphine equivalents taken in the two groups:  $42.8 \pm 43.9$  versus  $50.5 \pm 47.9$  mg, respectively (ns).
- Long-term ( $> 3$  months)
  - *Pain: there was no benefit* at twelve months (Table 17):
    - mean NRS scores (0-10 cm):  $3.5 \pm 1.2$  versus  $3.3 \pm 1.2$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 77% versus 77%, respectively (ns)
  - *Length of pain relief: there was no benefit* in the mean length of pain relief:  $37.7 \pm 15.4$  versus  $37.9 \pm 13.2$  weeks, respectively (ns).
  - *Function: there was no benefit* at twelve months (Table 17):
    - mean NDI scores (0-50 scale):  $13.8 \pm 5.5$  versus  $13.5 \pm 5.3$ , respectively (ns)
    - percent of patients achieving functional improvement of 50% or more: 71% versus 74%, respectively (ns)
  - *Opioid use: there was no benefit* at twelve months:  $41.6 \pm 44.9$  versus  $48.5 \pm 47.3$  mg (morphine equivalents), respectively (ns).
  - *Employment: there was no benefit* at twelve months in the percentage of those patients eligible for employment who were working part- or full-time: 75% versus 64%, respectively (ns).

**Table 17. Pain and function outcomes from trials of cervical epidural steroid injections versus placebo controls for neck pain with disc herniation and radiculitis**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results ( $\leq 3$ months)		Long-term results ( $> 3$ months)	
						Pain	Function	Pain	Function
Manchikanti	RCT	N = 120	Yes	Interlaminar	Epidural	Negative	Negative	Negative	Negative

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results ( $\leq 3$ months)		Long-term results ( $> 3$ months)	
						Pain	Function	Pain	Function
(2010) <sup>125</sup> (The effectiveness of fluoroscopic...)	LoE IIb			(n = 35)	local anesth. (n = 35)	(3 mos.)	(NDI) (3 mos.)	(12 mos.)	(NDI) (12 mos.)

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

***Neck pain without sciatica or radiculopathy***

One RCT<sup>124</sup> (LoE IIb) was identified and evaluated outcomes following fluoroscopically guided cervical interlaminar epidural injections with local anesthetic in the presence ( $n = 35$ ) or absence ( $n = 35$ ) of steroids in patients with chronic neck pain without disc herniation or radiculitis. Detailed demographic and outcome data are available in Appendix O.

Treatment (steroid) versus placebo (saline and/or local anesthetic) epidural injection:

- Short-term ( $\leq 3$  months):
  - *Pain: there was no benefit* associated with cervical epidural steroid injections (negative results) at three months (Table 18):
    - mean NRS scores (0-10 cm):  $3.1 \pm 1.0$  versus  $3.4 \pm 1.4$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 86% versus 77%, respectively ( $P = \text{NR}$ )
  - *Function: there was no benefit* at three months (Table 18):
    - mean NDI scores (0-50 scale):  $13.1 \pm 4.9$  versus  $15.1 \pm 5.9$ , respectively (ns)
    - percent of patients achieving functional improvement of 50% or more 80% versus 71%, respectively (ns)
  - *Opioid use: there was no benefit* at three months in the daily morphine equivalents taken in the two groups:  $36.1 \pm 23.9$  versus  $51.1 \pm 53.7$  mg, respectively (ns).
- Long-term ( $> 3$  months)
  - *Pain: there was no benefit* at twelve months (Table 18):
    - mean NRS scores (0-10 cm):  $3.2 \pm 1.1$  versus  $3.5 \pm 1.3$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 80% versus 80%, respectively ( $P = \text{NR}$ )
  - *Length of pain relief: there was no benefit* in the mean length of pain relief:  $39.7 \pm 13.6$  versus  $37.6 \pm 16.2$  weeks, respectively (ns).
  - *Function: there was no benefit* at twelve months (Table 18):
    - mean NDI scores (0-50 scale):  $12.7 \pm 4.9$  versus  $14.4 \pm 5.6$ , respectively (ns)
    - percent of patients achieving functional improvement of 50% or more: 80% versus 69%, respectively (ns)
  - *Opioid use: there was no benefit* at twelve months:  $36.4 \pm 23.9$  versus  $50.5 \pm 53.7$  mg (morphine equivalents), respectively (ns).
  - *Employment: there was no benefit* at twelve months in the percentage of those patients eligible for employment who were working part- or full-time: 79% versus 75%, respectively ( $P = \text{NR}$ ).

**Table 18. Pain and function outcomes from trials of cervical epidural steroid injections versus placebo controls for neck pain without disc herniation or radiculitis**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results (≤ 3 months)		Long-term results (> 3 months)	
						Pain	Function	Pain	Function
Manchikanti (2010) <sup>124</sup> (Cervical epidural injections...)	RCT  LoE IIb	N = 120	Yes	Interlaminar (n = 35)	Epidural local anesth. (n = 35)	Negative (3 mos.)	Negative (NDI) (3 mos.)	Negative (12 mos.)	Negative (NDI) (12 mos.)

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

#### 4.1.10 Cervical epidural injections versus non-placebo controls

One non-placebo controlled RCT<sup>193</sup> (LoE IIb) was identified. This study compared epidural to posterior neck intramuscular injections of steroid/local anesthetic in patients with chronic neck pain and resistant cervicobrachialgia. Detailed demographic and outcome data are available in Appendix O.

Treatment (steroid) versus intramuscular (steroid and local anesthetic) injection:

- Short-term ( $\leq 3$  months):
  - *Pain: epidural injections were superior* to intramuscular injections at one week as measured by the percent of patients who achieved pain relief of (Table 19):
    - 50% or more: 76% versus 35.2%, respectively ( $P = .004$ )
    - and-
    - 75% or more (very good): 44% versus 17.6%, respectively ( $P = .0377$ )
    - 50-74% (good): 32% versus 17.6%, respectively ( $P = \text{NR}$ )
    - 31-49% (satisfactory): 8% versus 23.6%, respectively ( $P = \text{NR}$ )
    - 30% or less (poor): 8% versus 29.4%, respectively ( $P = \text{NR}$ )
    - increase in the intensity of pain (worse): 8% versus 11.8%, respectively ( $P = \text{NR}$ )
  - *Analgesic use: epidural injections were superior* to intramuscular injections at one week in terms of the percent of patients with a decrease in their daily dose:
    - 81.7% versus 8.6%, respectively ( $P < .05$ )
  - *Employment: epidural injections were superior* to intramuscular injections at one week in terms of the percent of patients who had regained the ability to work:
    - 69.4% versus 12.8%, respectively ( $P < .05$ )
- Long-term ( $> 3$  months)
  - *Pain: epidural injections were superior* to intramuscular injections at 12 months as measured by the percent of patients who achieved pain relief of (Table 19):
    - 50% or more: 68% versus 11.8%, respectively ( $P = .0002$ )
    - and-
    - 75% or more (very good): 56% versus 5.9%, respectively ( $P = .0004$ )
    - 50-74% (good): 12% versus 5.9%, respectively ( $P = \text{NR}$ )
    - 31-49% (satisfactory): 20% versus 17.6%, respectively ( $P = \text{NR}$ )
    - 30% or less (poor): 4% versus 58.8%, respectively ( $P = \text{NR}$ )
    - increase in the intensity of pain (worse): 8% versus 11.8%, respectively ( $P = \text{NR}$ )
  - *Analgesic use: epidural injections were superior* to intramuscular injections at 12 months in terms of the percent of patients with a decrease in their daily dose:
    - 63.9% versus 9.4%, respectively ( $P < .05$ )
  - *Employment: epidural injections were superior* to intramuscular injections at 12 months in terms of the percent of patients who had regained the ability to work:
    - 61.3% versus 15.9%, respectively ( $P < .05$ )

**Table 19. Pain and function outcomes from trials of cervical epidural steroid injections versus non-placebo controls for neck pain with disc herniation and radiculitis**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results ( $\leq 3$ months)		Long-term results ( $> 3$ months)	
						Pain	Function	Pain	Function
Stav (1993) <sup>193</sup>	RCT	N = 50	No	NR (n = 25)	Posterior neck	Positive (1 week)	NR	Positive (12 mos.)	NR

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Epidural steroid injection approach (n)	Control (n)	Short-term results ( $\leq 3$ months)		Long-term results ( $> 3$ months)	
						Pain	Function	Pain	Function
	LoE IIb				intra-muscular steroid/ local anesth. (n = 25)				

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

### **SUMMARY: Efficacy of cervicalepidural steroid injections:**

- For trials comparing cervical epidural steroid injections with:
  - placebo injections for neck pain with disc herniation and radiculitis, there is no benefit based on data from one lower-quality RCT (strength of evidence = very low).
  - placebo injections for neck pain without disc herniation and radiculitis, there is no benefit based on data from one lower-quality RCT (strength of evidence = very low).
  - intramuscular injections for neck pain with disc compression and radiculitis, there is evidence that epidural injections were superior based on data from one lower-quality RCT (strength of evidence = very low).

#### 4.1.11 Cervical facet interventions versus placebo (saline and/or local anesthetic) controls

We identified one older RCT<sup>15</sup>, which received a LoE grade of IIb, that evaluated intraarticular injections with steroids/local anesthetic versus local anesthetic in patients with confirmed facet joint pain. The only outcome reported was the time to a return of 50% of baseline pain levels. Detailed demographic and outcome data are available in Appendix P.

##### *Intraarticular facet joint injections versus placebo controls*

Treatment (steroid) versus placebo (saline and/or local anesthetic) injection:

- Short-term ( $\leq 3$  months):
  - *Pain: there was no benefit* (negative results) (Table 20):
    - median time to a return to 50% of baseline pain levels: 3 versus 3.5 days (ns)<sup>15</sup>

**Table 20. Pain and function outcomes from placebo-controlled trials of cervical intraarticular facet joint injections**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Diagnostic block?	Control (n)	Short-term results ( $\leq 3$ months)		Long-term results ( $> 3$ months)	
						Pain	Function	Pain	Function
Barnsley (1994) <sup>15</sup>	RCT  LoE IIb	N = 42	Yes	Yes	Local anesth. (n = 20)	Negative	NR	NR	NR

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

##### *Therapeutic medial branch blocks versus placebo controls*

One RCT<sup>137</sup> compared outcomes following therapeutic medial branch blocks with local anesthetic in the presence or absence of steroid in patients with confirmed facet joint pain. The study received an LoE grade of IIb. Detailed demographic and outcome data are available in Appendix O.

Treatment (steroid) versus placebo (saline and/or local anesthetic) injection:

- Short-term ( $\leq 3$  months):
  - *Pain: there was no benefit* (negative results) at three months (Table 21):
    - mean NRS scores (0-10 cm):  $3.7 \pm 0.9$  versus  $3.8 \pm 1.0$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 87% versus 84% respectively (ns)
  - *Function: there was no benefit* at three months (Table 21):
    - mean NDI scores (0-50 scale):  $12.2 \pm 4.6$  versus  $12.0 \pm 5.2$ , respectively (ns)
- Long-term ( $> 3$  months):
  - *Pain: there was no benefit* (negative results) at 12 months (Table 21):
    - mean NRS scores (0-10 cm):  $3.4 \pm 0.9$  versus  $3.7 \pm 1.2$ , respectively (ns)
    - percent of patients achieving pain relief of 50% or more: 90% versus 90%, respectively (ns)
  - *Length of pain relief: there was no benefit* in the mean length of pain relief:  $48 \pm 6.2$  versus  $46 \pm 10.2$  weeks, respectively (ns)

- *Function: there was no benefit* at three months (Table 21):
  - mean NDI scores (0-50 scale):  $11.7 \pm 4.6$  versus  $11.7 \pm 5.0$ , respectively (ns)
- *Opioid use: there was no benefit* at twelve months:
  - none: 3% versus 7% of patients, respectively (ns)
  - mild intake (Schedule IV opioids (e.g., hydrocodone) up to 2 times/day): 0% versus 3% of patients, respectively (ns)
  - moderate intake (Schedule III opioids (e.g., hydrocodone) up to 4 times/day): 70% versus 70% of patients, respectively (ns)
  - heavy intake (Schedule II opioids (e.g., oxycodone or morphine) at any dose): 27% versus 20% of patients, respectively (ns)
- *Employment: there was no benefit* at twelve months in the percentage of those patients eligible for employment who were working part- or full-time: 86% versus 100%, respectively ( $P = \text{NR}$ )

**Table 21. Pain and function outcomes from placebo-controlled trials of cervical therapeutic medial branch blocks**

Study	Study type/ LoE	Sample size (N)	Fluor. guidance?	Diagnostic block?	Control (n)	Short-term results ( $\leq 3$ months)		Long-term results ( $> 3$ months)	
						Pain	Function	Pain	Function
Manchikanti (2008) <sup>137</sup> (Cervical medial branch blocks...)	RCT  LoE IIb	N = 120	Yes	Yes	Local anesth. (n = 60)	Negative (3 mos.)	Negative (NDI) (3 mos.)	Negative (12 mos.)	Negative (NDI) (12 mos.)

NR: not reported

Positive: the intervention is beneficial<sup>39, 40</sup>

Negative: the intervention is harmful or not beneficial<sup>39, 40</sup>

Unclear/mixed: imprecise estimates, unclear evidence, or inconsistent results<sup>39, 40</sup>

### **SUMMARY: Efficacy of cervicofacet joint interventions:**

- For trials comparing cervical intraarticular facet joint steroid injections with:
  - placebo injections for confirmed facet joint pain, there is no benefit based on data from one lower-quality RCT (strength of evidence = very low).
- For trials comparing cervical medial branch blocks with:
  - placebo injections for confirmed facet joint pain, there is no benefit based on data from one lower-quality RCT (strength of evidence = very low).

#### **4.1.12 Other potential comparisons**

Many studies included repeat, multilevel, and bilateral injections. However, we did not find any studies that compared repeat with single injections, multilevel with one-level injections, or bilateral with unilateral spinal injections.

## 4.2.Key Question 2: What is the evidence of the safety of spinal injections?

### 4.2.1. Complications following lumbar spine injections

#### **RCTs/SRs ≤ 2008:**

*Major complications:*Chou et al (2009)<sup>39, 40</sup> concluded that although major complications were rare in trials following lumbar epidural steroid injections, they were inadequately reported, with many trials not reporting complications at all. Summary rates of major complications were not given. One case of dural puncture was noted. The overall quality of evidence was considered to be poor. No major complications were reported for facet pain interventions, sacroiliac joint injections, or intradiscal injections.

*Minor complications:*Chou et al (2009)<sup>39, 40</sup> noted that adverse events following lumbar epidural injections tended to be transient and minor, and included pain at the injection site, headache, increased sciatic pain, nausea, pruritis, and irregular periods. There was one case of acute hypertension, and other of a retroperitoneal bleed in a patient on anticoagulation medications. The overall rate of minor complications was not reported. Transient pain at the injection site was also reported following facet joint injections; no complications were reported in studies that evaluated sacroiliac joint or intradiscal injections.

#### **RCTs ≥ 2008:**

*Major complications:*We assessed the 14 RCTs<sup>64, 99, 115-118, 132-136, 161, 176, 197</sup> included in Key Question 1 for information regarding the safety of lumbar spinal injections. Details are available in Appendix Q. Major complications were rare (we used patient numbers if the number of injections was not reported):

- **Dural puncture** occurred in 1/1556 injections or patients; the patient had received a interlaminar epidural injection, and no associated headache occurred (no other details were noted)<sup>136</sup>.
- **Subarachnoid puncture** also occurred in 1/1556 injections or patients; the patient had undergone an interlaminar epidural injection and did not experience a postprocedural headache<sup>116</sup>.
- **Angina pectoris** was reported for 1/1556 injections or patients; the patient subsequently dropped out of the study (no other details were reported)<sup>99</sup>.
- No deaths were attributed to spinal injection procedures. Death unrelated to the spinal injection occurred in 10/1146 patients.
- No other major adverse events were noted.

*Minor complications* also occurred infrequently, with 34 events reported in 1556 injections or patients<sup>99, 115-118, 132-136, 161, 176, 197</sup>. In general, these events tended to be transient in nature and included numbness in the lower extremities in the immediate postoperative period<sup>176</sup> (20/1556 injections or patients), vasovagal reactions/fainting<sup>176</sup> (12/1556 injections or patients), headache (without dural or subarachnoid puncture)<sup>116</sup> and gastric complaints<sup>99</sup> (1/1556 injections or patients each).

**Non-randomized studies/reports of complications:** We identified six studies<sup>25, 26, 32, 54, 122, 191</sup> that were designed primarily to evaluate the incidence of complications following injections into the lumbar spine. Follow-up ranged from procedural complications to those that occurred within three weeks post-procedure; most studies reported complications that occurred during or within a few days following the injection (see Appendix S for study details).

*Major complications* were rare, and included one case each of subarachnoid puncture and dural puncture (1/10,416 injections). No deaths were reported.

*Minor complications* were more common and again were generally transient in nature. An overall complication rate was presented in four<sup>25, 26, 122, 191</sup> of the six studies, and ranged from 2.7 – 16.3% of injections (mean: 5.8% of injections (176/3041)). Minor complications included (but were not limited to): headache, pain at injection site, increased leg pain or weakness, increased pain or new pain, facial flushing or rash, vasovagal reactions, blood sugar elevation, dizziness, nausea, and insomnia.

#### 4.2.2. Complications following cervical spine injections

##### **RCTs:**

*Major complications* following injections into the cervical spine were infrequent in the five RCTs evaluated for Key Question 1<sup>15, 124, 125, 137, 193</sup> (see Appendix R for details):

- **Subarachnoid puncture** was reported for 3/710 injections or patients (again, we used patient numbers if the number of injections was not reported); in all cases, the needle was removed and repositioned. Patients were treated with a caffeine infusion and did not experience any associated headache<sup>125</sup>.
- There were no reported instances of dural puncture (0/710 injections or patients).
- No deaths were reported for any of the 326 patients who underwent cervical spinal injections.
- No other major adverse events were noted.

*Minor complications* were also rare<sup>15, 124, 125, 137, 193</sup>; there were a total of 8 events reported for the 710 injections or patients who received cervical spine injections, including 6 cases of nerve root irritation<sup>124, 125</sup> and 2 cases of facial flushing<sup>15</sup> (Appendix R). All minor complications reported were transient in nature.

**Non-randomized studies/reports of complications:** Four studies<sup>111, 163, 179, 210</sup> met our inclusion criteria for non-randomized studies; adverse events were primarily reported in the immediate period following the injections, although some studies collected data for a few weeks. Detailed information is available in Appendix S.

##### *Major complications*

- Life-threatening generalized anaphylactic reaction (1/7240 injections or patients)<sup>179</sup>; the reaction occurred minutes following the nerve root block using a formulated steroid solution. The patient recovered fully.
- Grand-mal seizure: (1/7240 injections or patients)<sup>179</sup>. The seizure occurred within ten seconds of the steroid injection and lasted for 3-4 minutes; the patient had recovered completely within 30 minutes and was treated with nasal oxygen and intravenous saline.
- Dural puncture was reported in two patients (2/6330 patients)<sup>210</sup>; both patients experienced a positional headache when upright 24 hours after the procedure and received a cervical epidural autologous blood patch and recovered after another 24 hours of rest.
- Local hematoma (1/7240 injections or patients)<sup>163</sup>; the patient recovered fully.
- There were no reports of patient deaths.

*Minor complications:* One study reported an overall minor complication rate of 1.64% of injections (17/1036)<sup>111</sup>; minor complications included (but were not limited to) headache, dizziness, transient pain or weakness, vasovagal reactions, transient global amnesia, sympathetic blockade, increase in usual pain,

nausea, and superficial infections. These complications were uncommon and occurred in 0-3% of patients, although one study<sup>179</sup> reported that 10% of patients were experiencing increased clinical pain 10 days post-procedure.

#### 4.2.3. Complications following lumbar OR cervical spine injections

**Non-randomized studies/reports of complications:** Three non-randomized studies were identified that reported complications following lumbar or cervical spinal injections<sup>89, 92, 195</sup>. One study<sup>195</sup> collected only procedural data, the other two studies<sup>89, 92</sup> followed patients for up to three weeks (see Appendix S for details).

##### *Major complications:*

- Chest pain (1/6935 injections)<sup>195</sup>; the patient had a known chronic airway disease and was sent to the emergency room (no further details were reported).
- Tachycardia and hypertension (1/6935 injections)<sup>92</sup> occurred in one “mildly hypertensive” patient who required three days of hospitalization; the symptoms were attributed to steroid hypersensitivity.
- Significant transient hypotensive episode (1/6935 injections)<sup>92</sup>; the event occurred in an elderly patient who recovered fully and was released after two hours without further treatment.
- Hematoma (1/6935 injections)<sup>92</sup>; the hematoma developed at the injection site and extended up and down one segment but did not cause any spinal cord or nerve compression; the patient recovered within 18 hours and did not require any intervention.
- Dural puncture (1/6935 injections)<sup>89</sup> following a cervical nerve block; the patient did not experience a postprocedural headache.
- A severe vasovagal reaction occurred in one patient (1/6935 injections)<sup>92</sup>; the patient recovered and was discharged following three hours of observation in the emergency room
- No deaths were reported.

*Minor complications* were reported primarily in one study<sup>89</sup> but were difficult to distinguish from symptoms of the original spinal pain as symptoms were compared between patients who underwent lumbar or cervical selective nerve root injection to spinal pain patients who presented to the clinic but had not yet undergone spinal injection. Details can be found in Appendix S.

#### 4.2.4. Incidence of vascular puncture

We identified seven studies that prospectively<sup>62, 63, 70, 122, 123, 196</sup> or retrospectively<sup>195</sup> assessed the incidence of intravascular needle placement during spinal injection procedures (see Appendix T). Fluoroscopy was used to guide the placement of the needle in all but one<sup>123</sup> of the seven studies. The presence of flash or aspiration of blood in the needle hub was used as an indicator of intravascular needle placement. Actual needle position was evaluated by injecting contrast under live fluoroscopic visualization; the presence of vascular spread indicated intravascular needle placement. In the case of improper needle placement, the needle was subsequently repositioned in order to ensure correct placement prior to injection of the medication. Thus, these studies evaluated the incidence but not the consequences of intravascular injection.

Results are summarized in Appendix U. Briefly, the mean incidence of intravascular needle placement in 3526 fluoroscopically guided lumbar spinal injections was 10.2% (range, 1.9 to 22%) as reported in five studies, and that of 712 fluoroscopically guided cervical injections was 15.6% (range, 4.0 to 19.4%) from two studies. The mean sensitivity of flash/presence of blood in the needle hub or catheter as an indicator of intravascular needle placement was 44.3% from three studies evaluating lumbar injections and 45.9% from one study assessing cervical injections.

#### 4.2.5. Radiation exposure to the physician

Fluoroscopy is used in many medical procedures and facilitates correct needle placement and accurate delivery of injected medications in diagnostic and therapeutic spinal injections<sup>121</sup>. However, radiation exposure from the fluoroscope can pose a risk to the patient, physician, and other medical personnel. Physicians are most likely to have higher radiation exposure because of the cumulative effects of multiple procedures and are at higher risk for the resulting side effects<sup>121</sup>.

Radiation exposure is reported in REM (Roentgen Equivalent Man) or mREM (milliequivalent man) units and can be measured using a dosimetry badge<sup>79</sup>. The National Council on Radiation Protection and Measurements guidelines on the maximum annual permissible dose for occupational radiation exposure are as follows: whole body, 5 REM; lens of eye, 15 REM; extremities, 50 REM; and thyroid, 50 REM<sup>24, 119</sup>. Basic principles of radiation protection include maximizing the distance from the radiation source, the use of adequate shielding, and minimizing the exposure time<sup>119, 120</sup>. Physicians and other medical personnel are typically protected from radiation exposure by lead aprons, glasses, thyroid collars or shields, gloves, and drapes<sup>24, 119, 121</sup>.

We identified five studies that evaluated radiation exposure to the physician after performing a mean of 923 procedures (range, 100 – 1819) with an average length of radiation exposure of 9.8 seconds/procedure (range, 4.9 – 15.2)<sup>24, 27, 119-121</sup>. Total radiation exposure to the physician was within the range of normal limits in all five studies<sup>24, 27, 119-121</sup>. Exposure at the ring and glasses levels in two studies were 0.70 – 4.10 mREM/procedure and 0.39 – 2.47 mREM/procedure, respectively<sup>24, 27</sup>. Exposure outside the lead apron at chest level ranged from 0.30 – 3.98 mREM/procedure<sup>24, 27, 119-121</sup>. Two studies found exposure outside the apron at groin level ranging from 0.20 – 3.82 mREM/procedure<sup>120, 121</sup>. Exposure inside the lead apron was consistently less than outside the apron, with 0 – 0.15 mREM/procedure at chest level<sup>24, 27, 119, 120</sup>, 0 – 0.21 mREM/procedure at thyroid level<sup>120, 121</sup>, and 0 – 0.02 mREM/procedure at groin level<sup>120, 121</sup>. Factors influencing the cumulative radiation dose experienced by medical practitioners include the fluoroscopy mode used (intermittent/pulsed or continuous), the patient volume, the number of regions in the patient being treated, the experience of the physician and radiation technologist, and the type of shielding used<sup>121</sup>.

#### 4.2.6. Case reports of major adverse events following spinal injections

We found that major adverse events following spinal injections were relatively rare occurrences as reported in RCTs and case series of more than 100 patients. However, there have been numerous case reports of serious complications, including: spinal cord and/or cerebellar infarction<sup>16, 29, 68, 93, 109, 177, 200</sup> with varying consequences that ranged from short-term memory loss and difficulties concentrating<sup>16</sup> and transient quadriplegia<sup>93</sup> to paraplegia<sup>68</sup>, motor-incomplete tetraplegia<sup>109</sup>, quadriparesis<sup>200</sup>, and death<sup>29, 177</sup>; perforation of the left vertebral artery resulting in death<sup>174</sup>; generalized infection resulting in death<sup>97</sup>; extradural abscess<sup>72</sup> resulting in quadriplegia<sup>28</sup>; epidural abscess<sup>36</sup>; paraplegia<sup>86</sup>; discitis<sup>85</sup>; syrinx formation resulting in an inability to move right arm and leg<sup>96</sup>; permanent cervical cord damage<sup>84</sup>; anterior spinal artery

syndrome<sup>172</sup>; Cushing's syndrome<sup>203</sup> or transient hypercorticism<sup>192</sup>; chemical meningism<sup>199</sup> or severe meningitis<sup>52</sup>; extradural abscess<sup>72</sup>; retinal hemorrhage<sup>101</sup>; transient paralysis<sup>143</sup>; and cortical blindness and neurologic injury<sup>145</sup>. Because these complications appear to occur only in rare instances, large registry studies are needed in order to get an accurate estimate of the incidence of major complications following lumbar or cervical spinal injections. Smaller series have also suggested that epidural steroid injections may lead to insulin<sup>69, 211, 218</sup> and adrenal suppression<sup>103, 211, 218</sup>; further research is necessary to understand the frequency and potential implications of this effect.

### **SUMMARY: Safety of spinal injections**

- Major complications are rare following injections into the lumbar spine and included dural puncture, subarachnoid puncture, and chest pain. There were no cases of death or paralysis in the included studies, although there have been case reports of each in the published literature.
- Major complications are rare following injections into the cervical spine and included a life-threatening generalized anaphylactic reaction, grand-mal seizure, dural puncture, subarachnoid puncture, and local hematoma. There were no cases of death or paralysis in the included studies, although there have been case reports of each in the published literature.
- Other major complications were reported in case series of a mixture of lumbar and cervical spinal injection patients and included chest pain, tachycardia/hypertension, significant transient hypertensive episode, hematoma, dural puncture, and a severe vasovagal reaction.
- Minor complications are more common following lumbar or cervical spinal injections but are generally transient in nature, and include pain at the injection site, increased radicular pain/numbness/weakness, nerve root irritation, superficial infections, sympathetic blockade, facial flushing or rash, vasovagal reactions/fainting, headache, gastric complaints, dizziness, pruritis, irregular periods, and insomnia.
- The mean incidence of intravascular puncture following fluoroscopically guided lumbar spinal injections was 10.18% (range, 1.9–22%) as reported in five case series designed to assess its incidence (but not its consequences).
- With proper protective measures, total radiation exposure to the physician was within normal limits following a mean of 923 procedures (range, 100 – 1819) with an average length of radiation exposure of 9.8 seconds/procedure (range, 4.9 – 15.2) in all five case series we identified.

### **4.3.Key Question 3: What is the evidence that spinal injections have differential efficacy or safety issues in subpopulations?**

#### **4.3.1. Different approaches for administering lumbar epidural steroids in patients**

RCTs/SRs ≤ 2008: Chou et al (2009)<sup>39, 40</sup> reported mixed results with no approach clearly superior based on data from six trials (two higher-quality, four lower-quality) that directly compared different methods for administering epidural steroids. The transforaminal approach was found to be superior to both the interlaminar and caudal approaches in one higher-quality trial, but inconsistent results were reported comparing transforaminal versus interlaminar approaches in two lower-quality studies. One lower-quality trial found an oblique interlaminar approach modestly superior to a standard translaminar approach. Another lower-quality trial found no differences between the caudal and translaminar approaches. One higher-quality trial found no difference in outcomes comparing the caudal approach versus targeted steroid placement during spinal endoscopy in patients with radicular back pain, with needle placement confirmed by fluoroscopy for both methods.

Studies ≥ 2008: We found four studies comparing interlaminar versus transforaminal approaches published since the Chou SR, two RCTs<sup>33, 104</sup> and two retrospective cohort studies<sup>178, 183</sup>.

#### **Lee (2009)<sup>104</sup>**

In one RCT by Lee et al (2009)<sup>104</sup>, patients with axial back pain from a diagnosis of a herniated intervertebral disc (HIVD, n = 100) or spinal stenosis (n = 102) were randomly assigned to receive either interlaminar or bilateral transforaminal epidural steroid injections.

#### *Methodology (LoE IIb)*

Patients with unilateral or bilateral leg pain, arterial vascular disease, neurological deficits, previous spine surgery, or who had undergone lumbar epidural steroid injections within two months were excluded. Diagnoses were made from clinical exam and MRI findings. All injections were conducted under biplane fluoroscopic guidance using nonionic contrast medium. The total amount of injectate for each group was the same, 8 mL of lidocaine (0.5%) and 1 mL of triamcinolone acetonide (20 mg); however, patients in the bilateral transforaminal group received two injections of 4 mL lidocaine and 0.5 mL of triamcinolone, at the right and left neural foramina sequentially. Outcomes on the Numerical Rating Scale (NRS), the Patient Satisfaction Index (PSI), and the Roland 5-point pain score were reported at baseline, two weeks, two months, and four months after the last treatment. Complete follow-up was available in 95% of patients.

Authors report that randomization was carried out using a randomization table and that there were no significant differences in sex, age, and initial scores prior to intervention between the interlaminar and transforaminal groups in HIVD and spinal stenosis. All patients were evaluated by one physiatrist who was blinded to the approach used. Patients were also blinded to the technique they received. The authors do not state that an intention-to-treat analysis was performed or whether any cross-over between treatments occurred. If the patient's pain was level 5 or greater on the NRS at follow-up, they were reinjected at an interval of two weeks (maximum number of injections limited to three) but it is unclear whether or not the same approach was used at reinjection.

Patients not showing significant relief from injections or hoping to receive surgery were transferred to the surgical department. In some cases, these patients did not return and consequently were excluded

from the study (7% and 3% of the HIVD and spinal stenosis patients, respectively). Given that more patients with HIVD were transferred to the surgical department than spinal stenosis patients, exclusion of these patients would tend to overestimate the effect of epidural steroid injections among HIVD compared with spinal stenosis patients.

The authors reported that both the transforaminal and interlaminar epidural steroid injections accomplished pain reduction in HIVD and spinal stenosis patients at two weeks to four months follow-up. Among patients with a diagnosis of spinal stenosis, those receiving interlaminar epidural steroid did not fare as well as those receiving transforaminal epidural steroid injection for all three outcomes across each follow-up period, though not all comparisons reached statistical significance, Table 22. This level of evidence IIb study suggests that lumbar epidural steroid efficacy may be dependent in part on approach and diagnosis; that is, transforaminal injections may be more effective than interlaminar injections in patients with axial only pain from spinal stenosis, but not in patients with axial only pain attributed to herniated intervertebral discs.

**Table 22. Pain and satisfaction outcomes from one RCT<sup>104</sup> comparing epidural steroid injection administered by interlaminar (IL) versus transforaminal (TF) approaches stratified by diagnosis of herniated intervertebral disc (HIVD) or spinal stenosis (SS).**

	Change* in Roland Pain Score (%)				Patient Satisfaction Index (% successful†)				Change* in the Numerical Rating Scale for Pain (%)			
	2 weeks		4 months		2 weeks		4 months		2 weeks		4 months	
	IL	TF	IL	TF	IL	TF	IL	TF	IL	TF	IL	TF
HIVD	52.9	53.6	47.1	50.3	85.3	78.0	85.3	76.3	64.7	67.8	50.0	66.1
SS	33.8‡	52.8	33.8‡	47.2	64.3	75.4	52.4	66.7	35.7‡	54.4	31.0‡	50.9

\*change from baseline to follow-up

† defined as a the treatment met expectations or if not, the patient would undergo surgery again

‡  $P < .05$  comparing IF with TF reported by author

### **Candido (2008)<sup>33</sup>**

In another RCT by Candido et al (2008)<sup>33</sup>, 60 patients with low back pain and unilateral radiculopathy due to HIVD were randomly assigned to receive either parasagittal interlaminar or transforaminal epidural steroid injections.

#### **Methodology (LoE IIb)**

Patients with histories of previous spinal surgery, lumbar epidural steroid injections in the past year, allergy to drugs used, concurrent use of systemic steroid medications, opioid habituation, and pregnancy were excluded. Biplane fluoroscopic guidance was used in all cases with a total volume of nonionic contrast material of 5.0 mL. Methylprednisolone acetate 80 mg, normal saline 1 mL, and lidocaine (1%) 1 mL, were injected for a total volume of injectate of 4 mL. The primary purpose of this study was to compare contrast flow patterns in the epidural space using interlaminar versus transforaminal approaches, and the study powered to detect this outcome. The clinical outcome of pain relief (VAS), the main focus of this report, was considered a secondary outcome and was reported at two weeks, one month, three months, and six months. Complete follow-up was available in 95% of patients.

Randomization was achieved using a computer-generated randomization table and demographics (age, height, weight) were similar between the two groups at baseline. However, there was a difference in VAS scores between groups at baseline (interlaminar = 67.9; transforaminal = 63.2) which was not accounted for in the analysis. The authors state that an independent and blinded radiologist reviewed

the scoring of the degree of contrast spread. However, it is not clear whether the collection and evaluation of VAS scores was completed in a blinded fashion or whether patients were blinded to the approach they received. Bias arising from the lack of blinding is possible. The authors do not state that an intention-to-treat analysis was performed. Of the patients, 15 who received interlaminar and 12 who received transforaminal crossed-over to the other group at some point during the study. Furthermore, three patients were excluded after random assignment, two in the transforaminal group due to the inability to place the needle tip in the correct location within the allotted fluoroscopy time, and one in the interlaminar group due to an aborted procedure secondary to pain with needle insertion.

As discussed by the authors, since only the first intervention was controlled for each patient, their ability to draw reliable outcomes conclusions in many cases as to the efficacy of one technique over the other was limited. Nonetheless, the results of this study demonstrated no statistical difference in changed pain score from baseline at two weeks comparing interlaminar with transforaminal approaches (40.2% improvement versus 22.7%, respectively), at three months (31.3% improvement versus 32.1%, respectively), and at six months (39.3% improvement versus 25.5%, respectively).

### ***Smith (2010)<sup>183</sup> & Schaufele (2006)<sup>178</sup>***

The two retrospective matched cohort studies<sup>178, 183</sup> (LoE III) report different results from the RCTs. Smith et al (2010)<sup>183</sup> compared the interlaminar with the transforaminal approach in patients with spinal stenosis and found no difference in the proportion of patients having  $\geq 50\%$  decrease in pain (36.8% versus 31.6%), the proportion of patients going on to surgery (10.5% versus 15.8%) or the proportion of patients receiving repeat injections (26.3% versus 15.8%). On the other hand, Schaufele et al (2006)<sup>178</sup> reported worse pain assessments in those receiving interlaminar epidural steroid injections compared with transforaminal in patients with HIVD (45% of interlaminar patients improved 2+ points on the numerical rating scale (NRS) compared with 70% of transforaminal patients,  $P < .01$ ). There were no statistical differences in the proportion of patients going on to surgery (25% versus 10%) or the proportion of patients receiving repeat injections (60% versus 55%).

**Summary:** There is no consistent evidence from a systematic review of six RCTs and two additional RCTs published since the systematic review that one approach is more efficacious/effective in administering lumbar epidural steroid. The results of one lower quality RCT suggest that interlaminar injections may not be as effective as transforaminal in patients with axial only pain from spinal stenosis. However, more study is needed to verify these findings.

### **4.3.2. Diagnosis**

In addition to the Lee et al (2009)<sup>104</sup> study mentioned above, two prognostic studies evaluated whether diagnosis was associated with outcome in patients receiving lumbar epidural steroid injections. One reported that a diagnosis of lumbar spinal stenosis was associated with less improvement in pain from baseline than HIVD following lumbar epidural steroid injection ( $P = .03$ )<sup>169</sup>. The approach was not specified in this study. A second retrospective cohort study<sup>105</sup> conducted via a medical records review of all patients undergoing lumbar transforaminal epidural steroid injections reported no difference in effective outcome (reduction in VAS pain score of  $> 50\%$  and a patient satisfaction score of “very good” or “excellent”) between patients with spinal stenosis and HIVD.

Two retrospective studies assessed cervical epidural steroid injections, one of which found a significant improvement in pain for patients with herniated intervertebral discs (HIVD) versus those with spinal stenosis following an interlaminar approach, 86.1% versus 60.0%, respectively ( $P = .01$ )<sup>102</sup>. The second study did not specify the approach used for cervical epidural steroid injections but reported that patients

with cervical radiculopathy tended to respond better with regards to pain improvement and return to normal activities of daily living versus those with radiculitis or spondylitis, 62% and 61% versus 35%, though this difference did not reach statistical significance ( $P = .06$ )<sup>57</sup>.

**Summary:** There is no consistent evidence that epidural steroid injections have differential efficacy or effectiveness among various diagnoses of the lumbar or cervical spine.

#### 4.3.3. Baseline pain and dysfunction

We identified four studies that evaluated baseline pain intensity or duration and dysfunction as predictors of success with epidural steroid injections.

One LoE IIB RCT<sup>64</sup> (included in key question 1; critically appraised in section 3.2.3) evaluated whether there was an association between chronicity of pain and pain relief following transforaminal steroid injections compared with placebo (transforaminal injections of local anesthetic or saline) or non-placebo controls (intramuscular injections of local anesthetic or saline). No differences were found between patients with acute ( $< 3$  months; median of each treatment group ranged from 3 – 8 weeks) versus chronic ( $\geq 3$  months, median of each treatment group ranged from 32 – 96 weeks) pain in terms of the percent of patients achieving pain relief of at least 50% at one month in any of the treatment groups: transforaminal steroid (47% (acute) versus 55% (chronic)), local anesthetic (0% versus 13%, respectively), or saline (24% versus 13%, respectively) injections; intramuscular steroid (25% versus 19%, respectively) or saline (7% versus 20%, respectively) injections.

One prospective cohort reported that patients with higher (worse) baseline VAS pain scores experienced greater improvement in pain than those with lower baseline scores following lumbar epidural steroid injections ( $P < .001$ ), as did patients who reported a greater degree of difficulty doing chores pre-injection than those who had less difficulty with chores at baseline ( $P < .001$ )<sup>169</sup>. However, this study had a follow-up rate of only 37% which makes the results suspect. No association was found in three retrospective cohort studies between pre-injection pain duration and outcome in lumbar or cervical interlaminar epidural steroid injections ( $< 3$  months versus  $> 3$  months<sup>106</sup>, or  $< 6$  months versus  $> 6$  months<sup>102, 105</sup>).

#### 4.3.4. Injectate

Dreyfuss et al (2006) conducted an RCT that compared patients undergoing cervical transforaminal epidural steroid injections with either dexamethasone 12.5 mg ( $n = 15$ ) or triamcinolone acetate 60 mg ( $n = 15$ )<sup>53</sup>. The primary purpose of this LoE IIB article was to determine whether a nonparticulate corticosteroid preparation (dexamethasone) is any less effective than a common particulate corticosteroid preparation (triamcinolone). Patients with other pain or a comorbid condition that might interfere with assessment of relief of the radicular pain and central spinal stenosis less than 8 mm were excluded. Fluoroscopic guidance was used in all cases and 0.75 to 1.0 mL of lidocaine 4% was injected just prior to corticosteroid injection. The primary outcome measure was the percentage reduction of pain (VAS) at four weeks follow-up. A patient-reported functional outcome which assessed pre-treatment limitations in activities of daily living important to an individual patient and whether or not they regained the ability to perform specific activities post-injection was used as a secondary outcome measure. Additionally, work status was assessed before and after treatment. Complete follow-up was reported in 100% of patients. VAS ratings were obtained by an

“independent, unbiased assessor”. There is no indication that the patients were blinded to the treatment they received. The authors do not state that an intention-to-treat analysis was performed or whether any cross-over between treatments occurred.

The investigators found no statistical difference in the proportion of patients reporting 100% relief in pain for dexamethasone compared with triamcinolone (27% versus 7%) or 50% relief in pain (69% versus 67%). There were no differences reported between patients in various age groups.

#### 4.3.5. Other

Sex and age were evaluated as potential prognostic factors in three retrospective studies, two on patients who received lumbar epidural steroid injections (via the interlaminar approach in one and the transforaminal approach in another)<sup>105, 106</sup> and one on patients who underwent cervical interlaminar epidural steroid injections<sup>102</sup>. Neither sex nor were found to be associated with outcome in any of the studies.

One retrospective study on lumbar interlaminar epidural steroid injection patients looked at whether the presence or absence of various MRI findings predicted patient outcome in terms of a greater than 50% improvement in VAS pain score and patient satisfaction (NASS patient satisfaction index). No significant associations were reported between any of the MRI findings and outcome in this study<sup>106</sup>.

Another retrospective cohort compared saddle-type contrast distributions to non-saddle-type distributions during lumbar transforaminal epidural steroid injections and found no association between these two contrast distribution patterns and an effective outcome in terms of pain improvement and patient satisfaction<sup>105</sup>.

**Summary:** There is no consistent evidence that pre-injection pain intensity or duration, type of steroid used as injectate, sex, age or pre-injection MRI findings are associated with outcome in patients receiving epidural steroid injections of the lumbar or cervical spine.

#### ***4.4.Key Question 4:What is the evidence of cost implications and cost-effectiveness of spinal injections?***

##### **4.4.1. Background and context**

Economic evaluations identify and compare appropriate alternatives, their incremental impact on health outcomes, and their incremental costs. There are several types of economic evaluation. Cost minimization studies consider the cost differences between alternatives of equal effectiveness. Cost benefit studies consider both costs and benefits in monetary terms. Cost effectiveness studies consider differences in costs and differences in effectiveness, but effectiveness is measured variably between studies (e.g., can be survival or a condition-specific outcome such as symptom-free days). Cost utility studies consider differences in costs and outcomes for quality-adjusted survival, most often using the quality adjusted life year (QALY). Cost utility studies have the advantage of providing an incremental cost effectiveness ratio (ICER) expressed as ‘cost per quality adjusted life year’ (cost per QALY) that eases comparison across multiple studies. Studies that report only costs or do not compare alternatives are not considered full economic evaluations.

When evaluating the quality of economic evaluations, we use the Quality of Health Economics Studies (QHES)<sup>156</sup>, which allows rating of study methodology, perspective, time horizon, uncertainty analysis, model inputs of both costs and outcomes (in the absence of long-term data from a randomized trial, modeling methods are often employed), and statement of funding. We also assess the quality of the clinical data in economic studies vis a vis the evidence for efficacy and effectiveness in other sections of this report.

Following our decision to use a comprehensive 2009 evidence report (Chou)<sup>39, 40</sup> as the basis for the lumbar portion of this efficacy review, we used the same review as the basis of our assessment of economic evidence. In that report, cost studies conducted alongside randomized controlled trials or full economic evaluations were included. Two studies were appropriate for inclusion both by our criteria and by the report (Price et al (NHS HTA) (2005)<sup>164</sup>, Karppinen et al (2001)<sup>94</sup>), both on epidural steroid injections. No additional economic studies on lumbar facet injections, lumbar medial branch blocks, sacroiliac joint injections, or lumbar intradiscal injections were identified, either in the 2009 evidence report (Chou)<sup>39, 40</sup> or published in/after 2008. No economic studies were identified that evaluated any type of cervical spinal injection.

Details of the two included studies can be found in Appendix V.

## Washington State Data

**Figure 1: Combined Agency Costs and Counts, 2006-2009**

Agency/Year		2006	2007	2008	2009	4 year Totals
<b>UMP/PEP Overall</b>	Direct Costs	\$1,385,787	\$1,577,866	\$2,174,039	\$2,514,318	\$7,652,010
	Procedures	6815	7586	9758	11371	35530
	Claimants	1786	2008	2493	2806	9093**
	Avg Proc Cost*	\$203	\$208	\$223	\$221	\$215
	Avg Claimant Cost*	\$776	\$786	\$872	\$896	\$842**
<b>UMP/PEP Primary</b>	Direct Costs	\$1,338,638	\$1,517,066	\$2,114,366	\$2,401,196	\$7,371,266
	Procedures	3447	3797	5352	6324	18920
	Claimants	937	1070	1403	1611	3830**
	Avg Proc Cost*	388	400	395	380	390
	Avg Claimant Cost*	1,429	1,418	1,507	1,491	1,925**
<b>UMP/PEP Secondary</b>	Direct Costs	\$47,149	\$60,800	\$59,673	\$113,122	\$280,744
	Procedures	3368	3789	4406	5047	16610
	Claimants	849	938	1090	1195	5263**
<b>DLI</b>	Direct Costs	\$10,413,407	\$10,385,032	\$10,764,742	\$10,561,981	\$42,125,162
	Procedures	20208	19714	22117	24132	86171
	Claimants	4667	4414	4608	4887	18576
	Avg Proc Cost	\$515	\$527	\$487	\$438	\$489
	Avg Claimant Cost	\$2,231	\$2,353	\$2,336	\$2,161	\$2,268
<b>DSHS</b>	Direct Costs	\$1,321,088	\$1,333,749	\$1,520,215	\$1,770,666	\$5,945,718
	Procedures	7275	6694	7792	8625	30386
	Claimants	2557	2650	2924	3385	9177**
	Avg Proc Cost	\$182	199	195	205	196
	Avg Claimant Cost	\$517	\$503	\$520	\$523	\$648**
<b>All Agencies Combined</b>	Direct Costs	\$13,120,282	\$13,296,646	\$14,458,996	\$14,846,966	\$55,722,890
	Procedures	34298	33994	39667	44128	152087
	Claimants	9010	9072	10025	11078	36846
	Avg Proc Cost	\$383	\$391	\$365	\$336	\$366
	Avg Claimant Cost	\$1,456	\$1,466	\$1,442	\$1,340	\$1,512

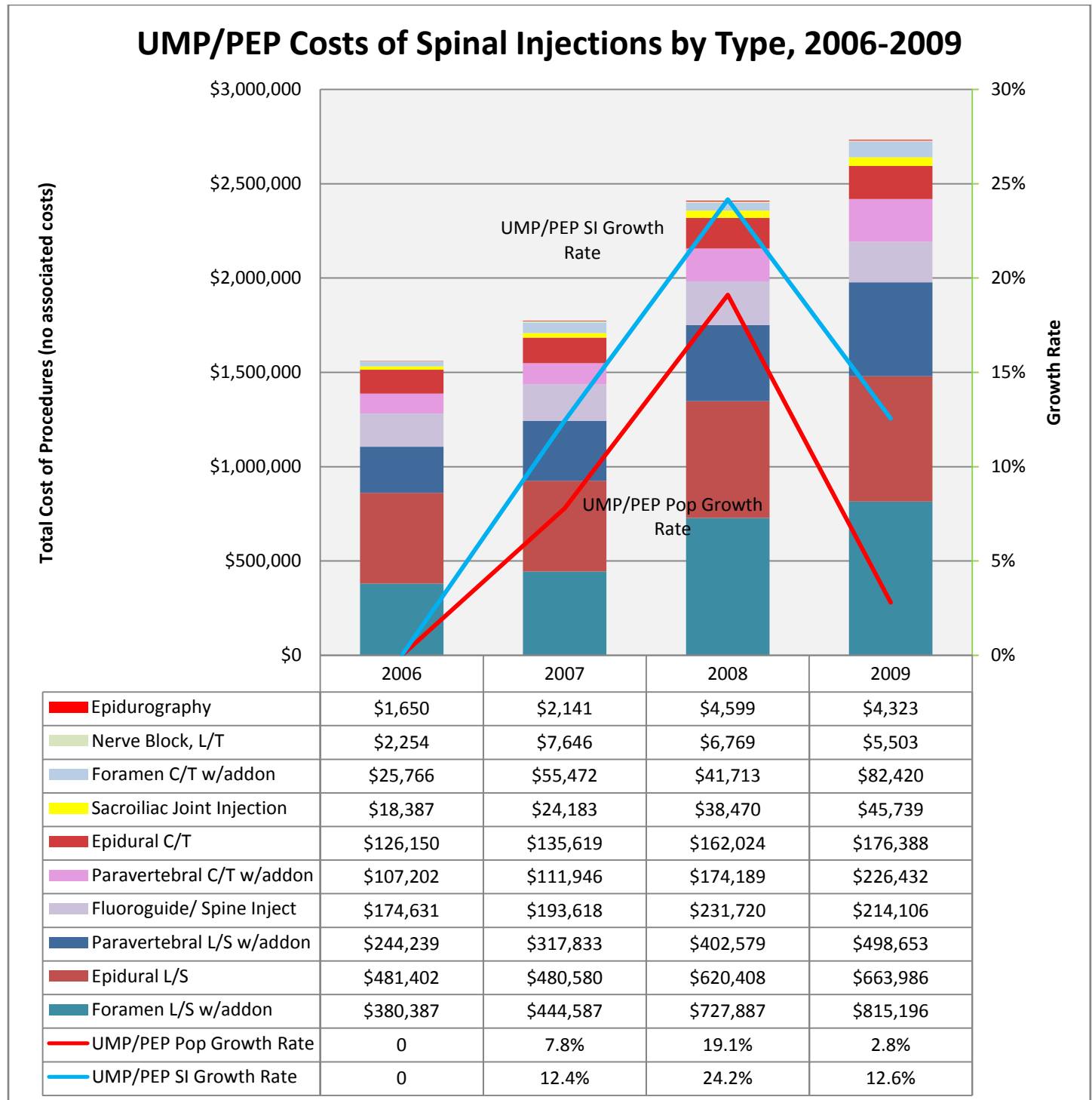
\*UMP Averages calculated using overall UMP/PEP counts and costs shown are artificially low due to the inclusion of members where UMP/PEP is the secondary payer. More representative costs are shown in the UMP/PEP Primary Payer averages.

\*\*4 year total claimant counts for DSHS and UMP/PEP reflect distinct members, not the total of 2006-2009 claimant counts - therefore the 4 year average claimant cost reflects the cost per each distinct claimant over 4 years

\*\*\*All Agency Combined Direct Costs is the total of the separate agency sections above, except UMP/PEP subsections (Primary vs Secondary shown in gray).

Note: Direct costs are those paid on identified CPT codes for spinal injection procedures.

Figure 2a: UMP/PEP Costs for Spinal Injection by Type, 2006-2009



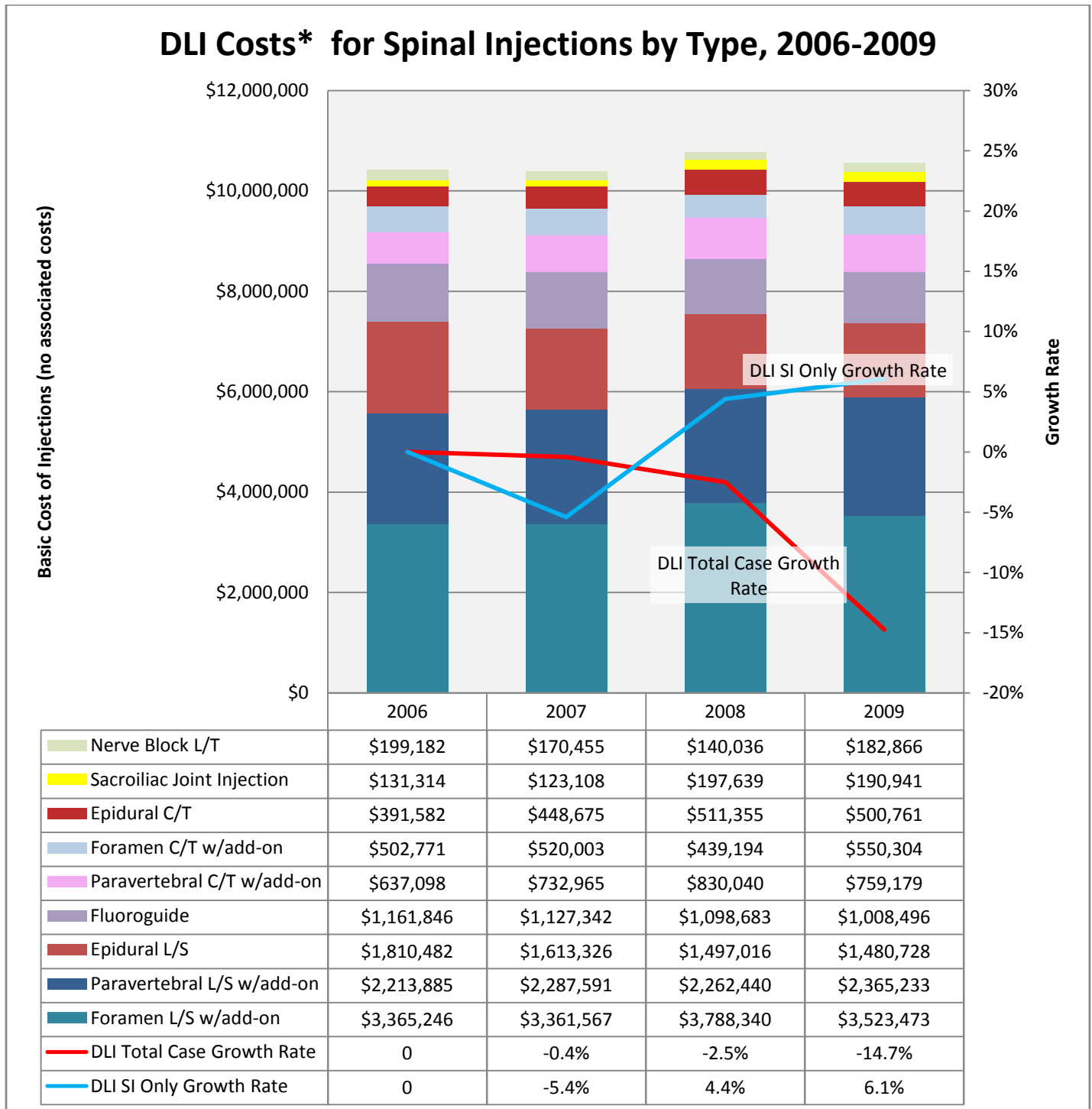
\*Only direct procedure costs (CPT) were used (no associated costs). Add-on code costs were combined with the main code.

**Abbreviations:**

SI = Spinal Injections (all injections under review)

L/S = Lumbar/Sacral, C/T = Cervical/Thoracic – indicating different spinal levels in the reimbursement codes for some procedures.

Figure 2b: DLI Costs for Spinal Injections by Type, 2006-2009



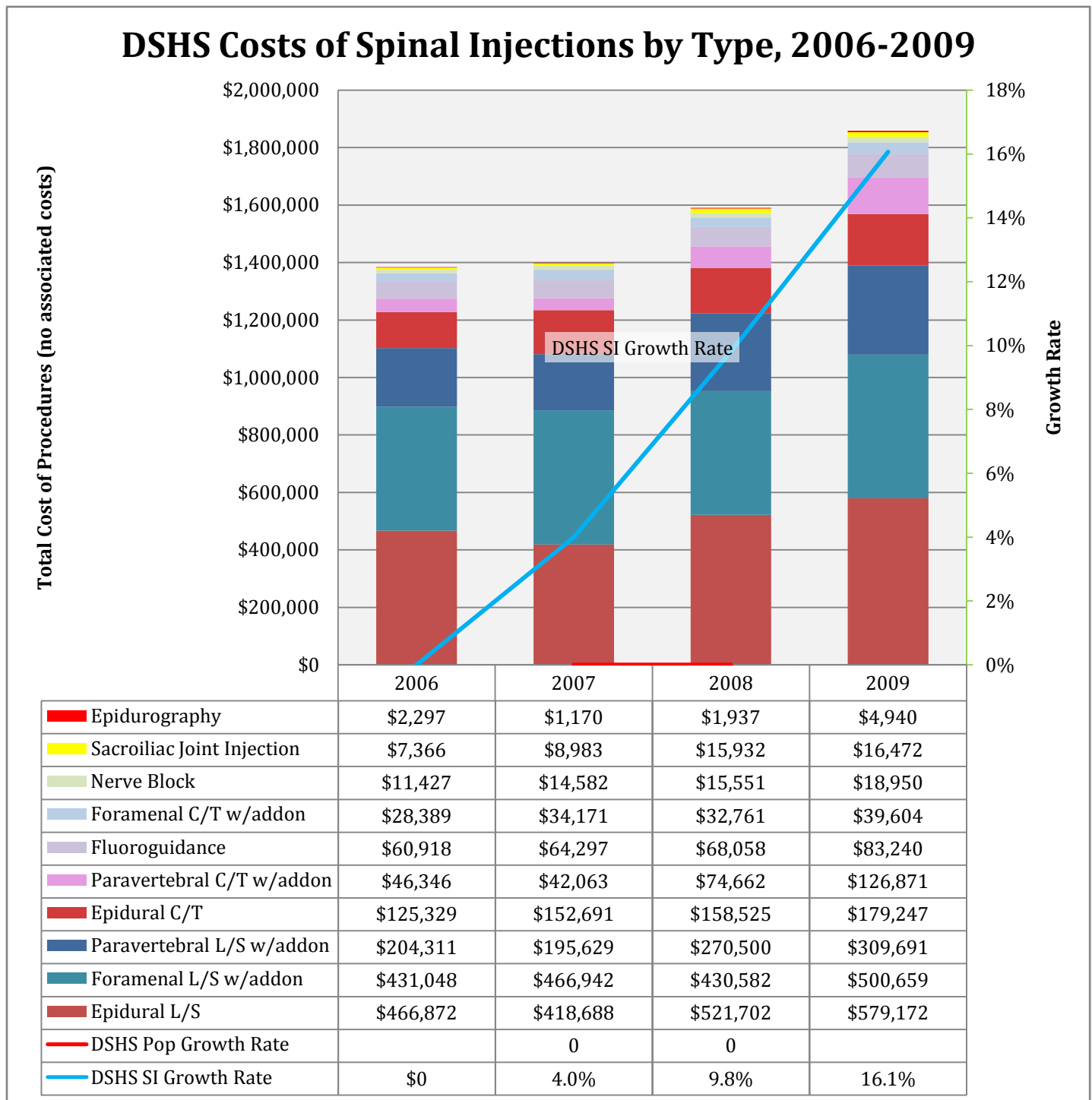
\*Only direct procedure costs (CPT) were used (no associated costs). Add-on code costs were combined with the main code.

Abbreviations:

SI = Spinal Injections (all injections under review)

L/S = Lumbar/Sacral, C/T = Cervical/Thoracic – indicating different spinal levels in the reimbursement codes for some procedures

Figure 2c: DSHS Costs for Spinal Injections by Type, 2006-2009



\*Only direct procedure costs (CPT) were used (no associated costs). Add-on code costs were combined with the main code.

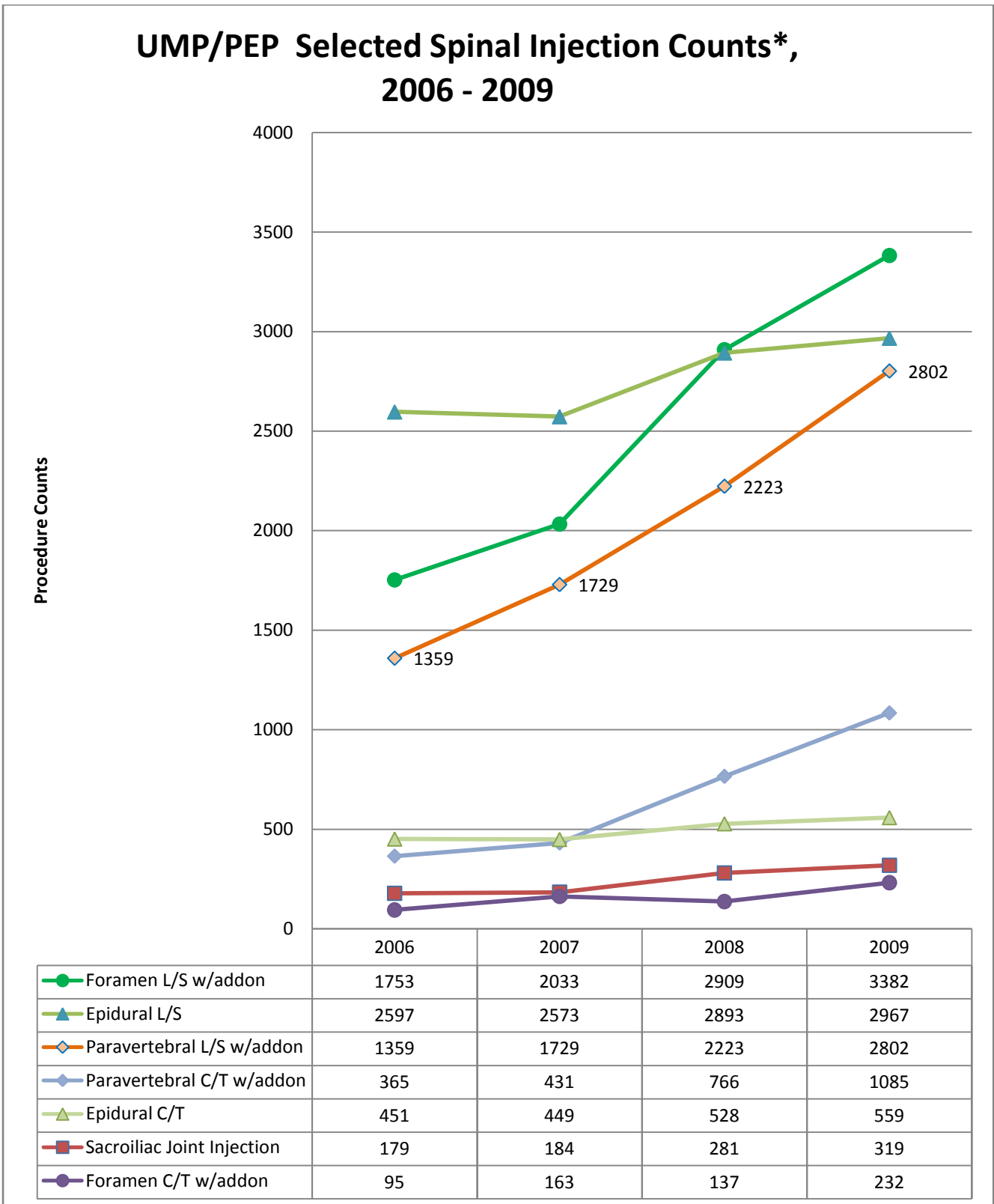
Note that population growth rates for DSHS 2006-2009 were not available

Abbreviations:

SI = Spinal Injections (all injections under review)

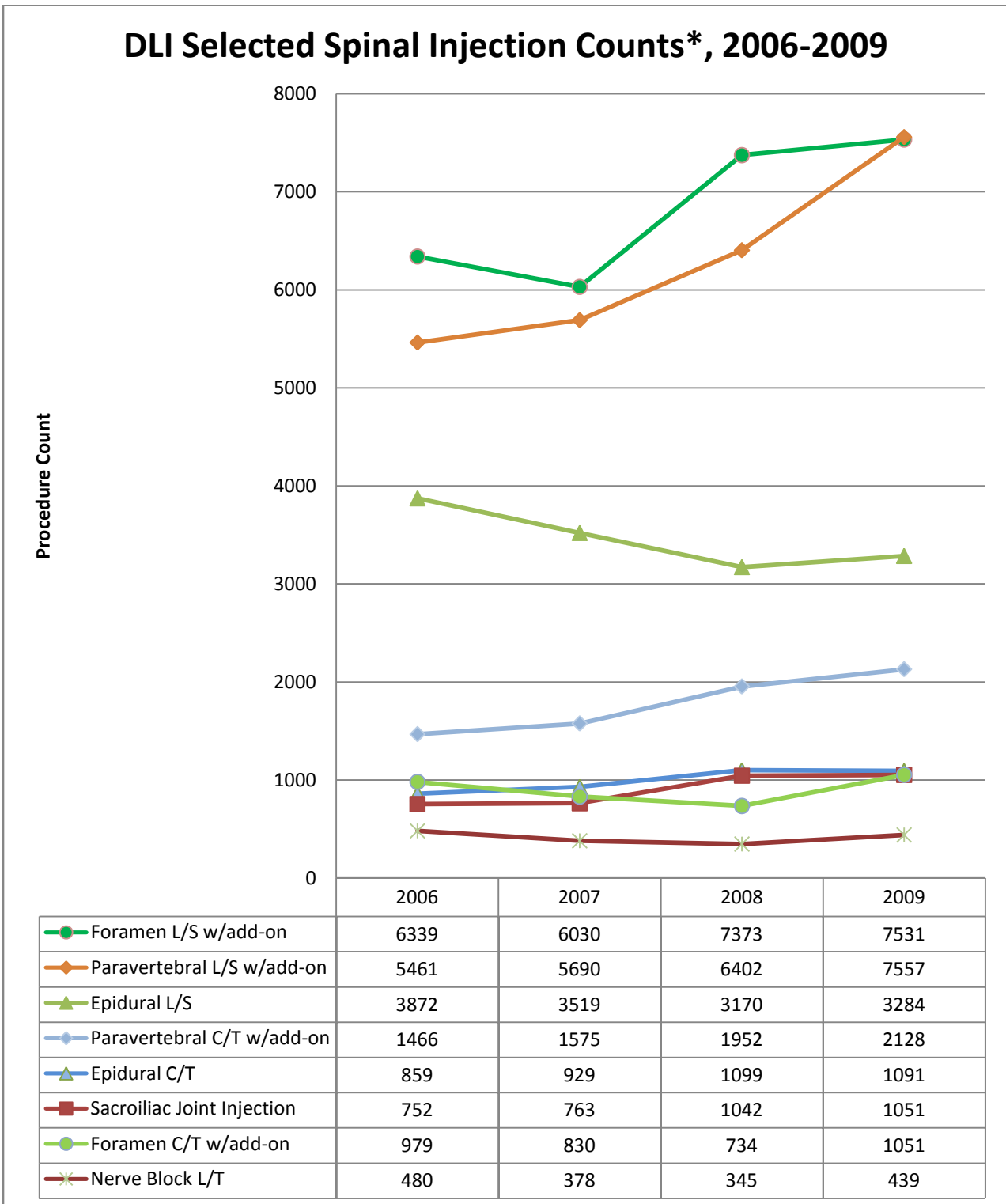
L/S = Lumbar/Sacral, C/T = Cervical/Thoracic – indicating different spinal levels in the reimbursement codes for some procedures

Figure 3a: UMP/PEP Selected Spinal Injection Counts, 2006-2009



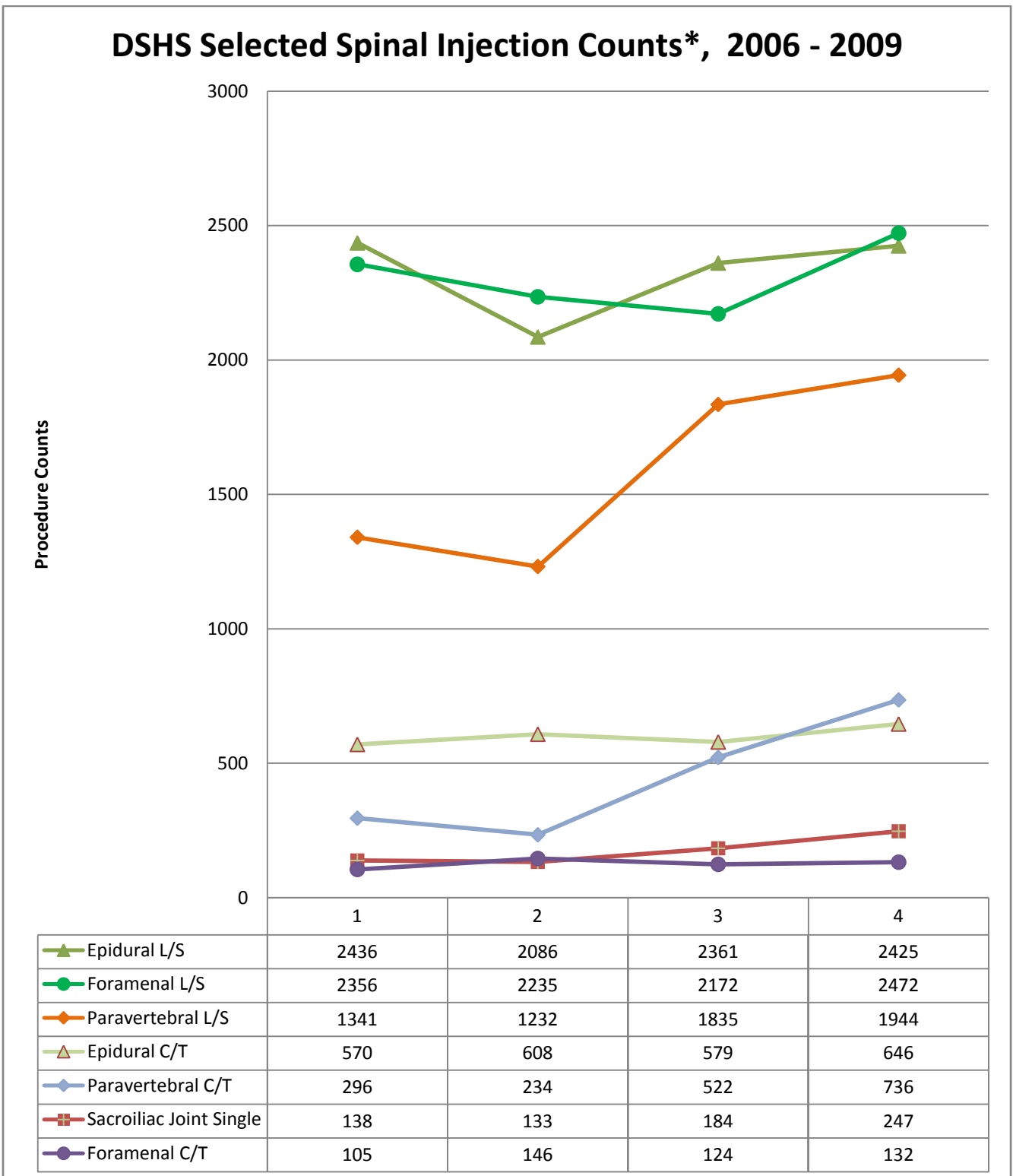
\*Procedures were consolidated to count as a single procedure when a professional and facility charge with the same CPT code occurred on the same day. All injections, including "additional level" injections were counted.

Figure 3b: DLI Selected Spinal Injection Counts, 2006-2009



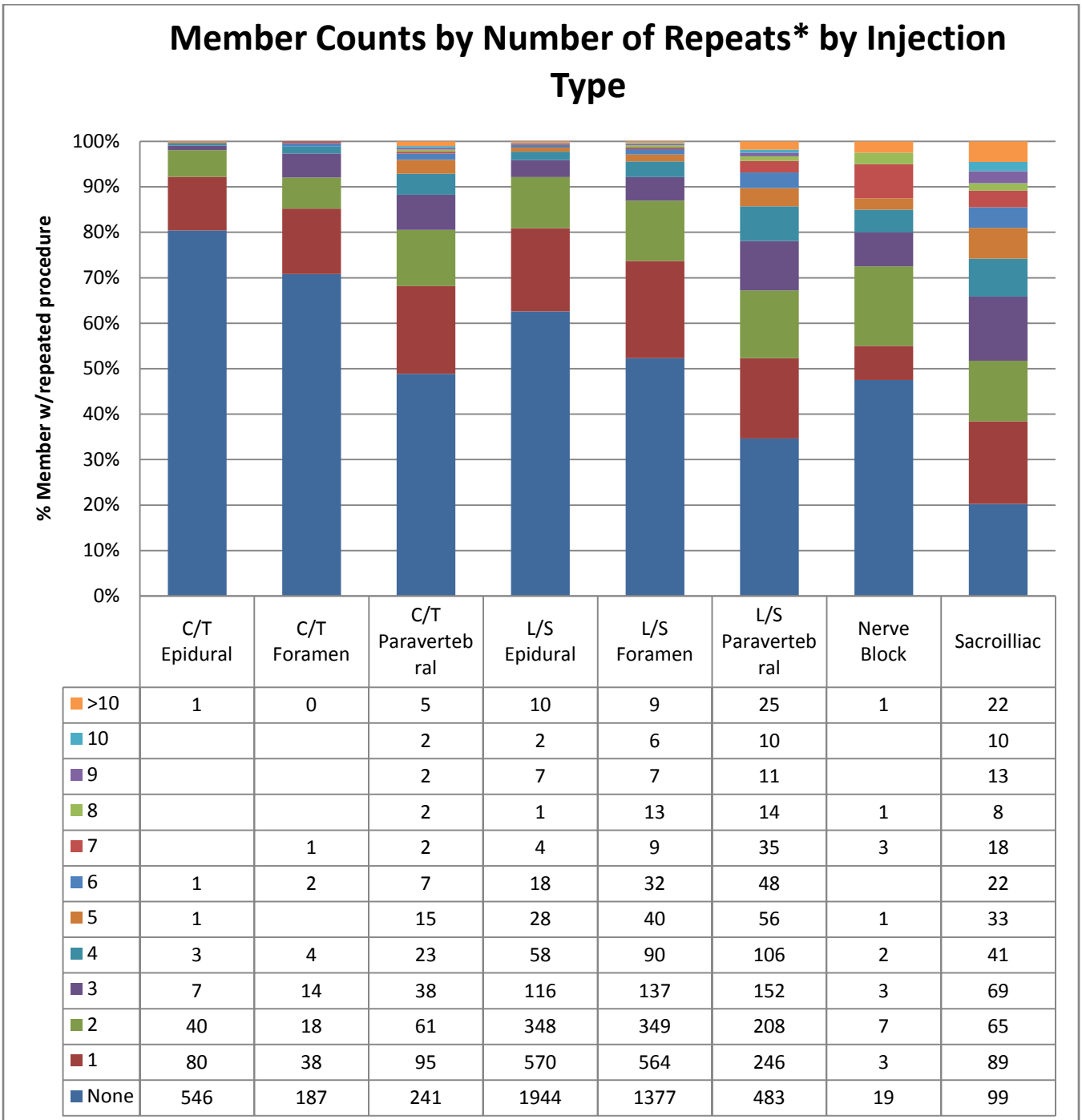
\*Procedures were consolidated to count as a single procedure when a professional and facility charge occurred on the same day. All injections, including "additional level" injections were counted.

Figure 3c: DSHS Selected Spinal Injection Counts, 2006-2009



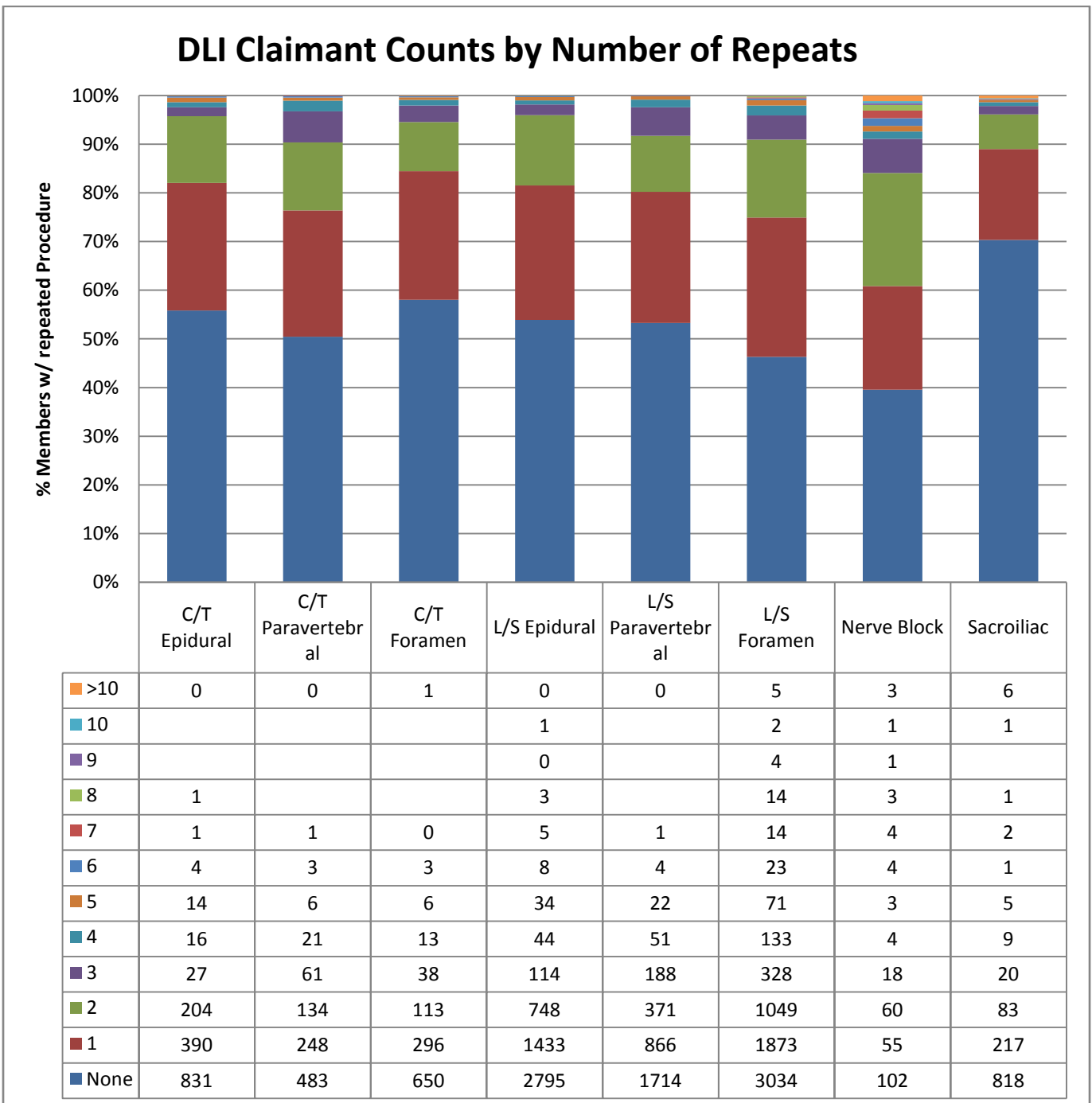
*\*Procedures were consolidated to count as a single procedure when a professional and facility charge occurred on the same day. All injections, including "additional level" injections were counted.*

Figure 4a. UMP/PEP Members by Repeat Counts/Spinal Injection Type, 2006-2009



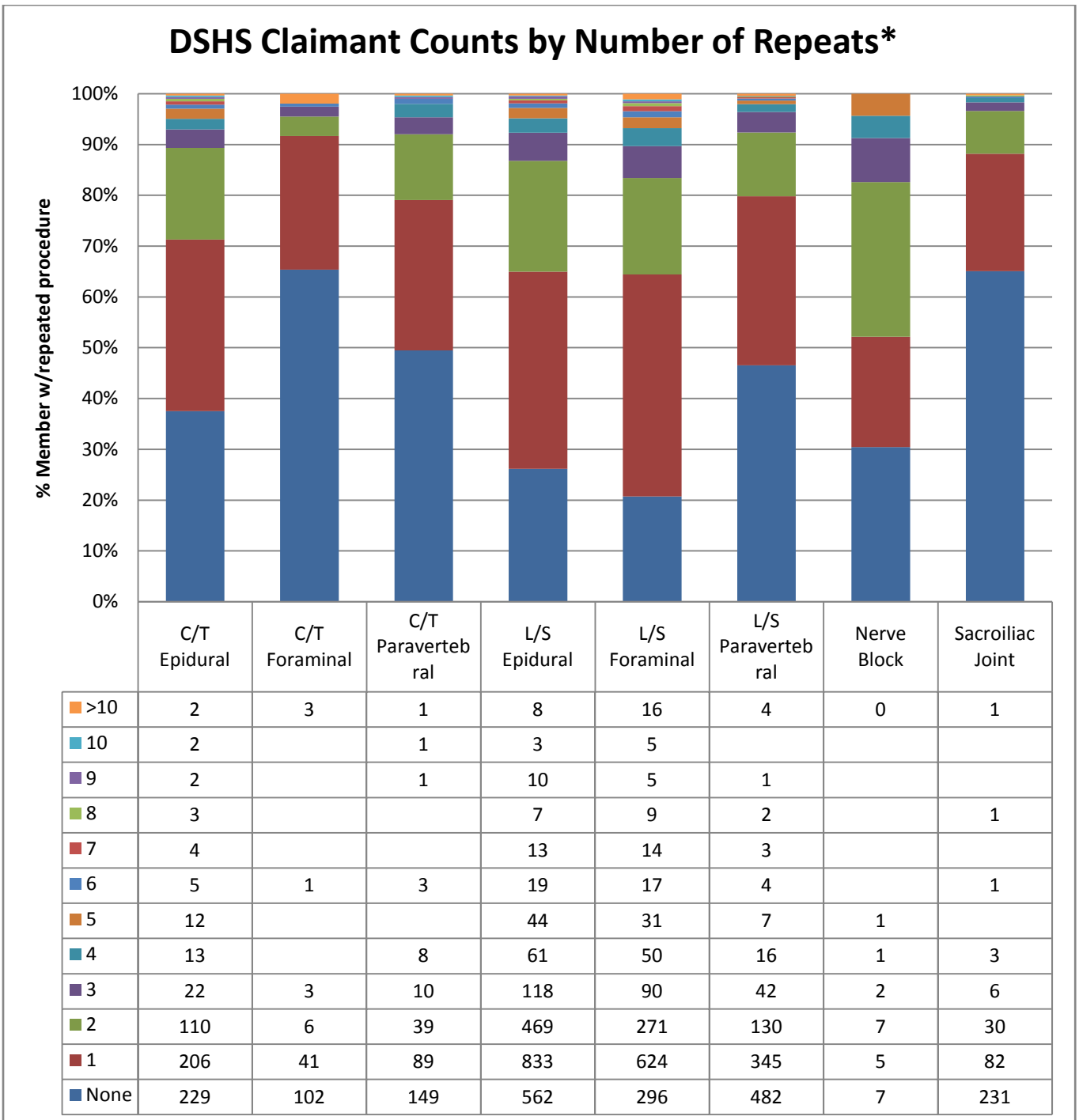
\*Chart modified 2/25/2011 due to over reporting of patients having only a single procedure, and some procedures counted in the wrong column when a single patient had multiple procedures of more than one type.

Figure 4b. DLI Members by Repeat Counts/Spinal Injection Type, 2006-2009



\*Chart modified 2/25/2011 due to over reporting of patients having only a single procedure, and some procedures counted in the wrong column when a single patient had multiple procedures of more than one type.

Figure 4c. DSHS Claimants by Repeat Counts/Spinal Injection Type, 2006-2009



\*Chart modified 2/25/2011 due to over reporting of patients having only a single procedure, and some procedures counted in the wrong column when a single patient had multiple procedures of more than one type.

**Figure 5a: UMP/PEP Spinal Injection Repeat Procedure Table, 2006-2009**

NOTE: Table modified 2/25/2011 due to miscounts of members with multiple procedures on different days – members with multiple procedures of different types were counted under the category of the final procedure, requiring corrections to both procedure and member counts - Columns modified: 8-13

Injection		Average procedure count per member			Same day multiple Procs		Different day repeated procedures					
Level	Type	Proc ct	Mbr ct	Average	Proc ct	% Procs	Proc ct	Mbr ct	% Mbrs	Avg Proc Days/ Mbr	Max Procs/ Mbr	Avg days between procs
C/T	Epidural	1987	679	2.9	812	40.9%	732	133	11.6%	5.5	12	74.0
	Foraminal	627	264	2.4	239	38.1%	171	77	21.1%	2.2	7	38.0
	Paravertebral	2647	493	5.4	749	28.3%	665	252	26.8%	2.6	27	43.1
<b>Total C/T</b>		<b>5261</b>	<b>1436</b>	<b>3.7</b>	<b>1800</b>	<b>34.2%</b>	<b>1568</b>	<b>462</b>	<b>18.9%</b>	<b>3.4</b>		<b>56.9</b>
L/S	Epidural	11030	3106	3.6	4318	39.1%	5114	1162	17.8%	4.4	33	72.0
	Foraminal	10077	2633	3.8	3422	34.0%	3753	1256	24.8%	3.0	16	69.6
	Paravertebral	8113	1394	5.8	2184	26.9%	1981	911	33.8%	2.2	54	51.1
<b>Total L/S</b>		<b>29220</b>	<b>7133</b>	<b>4.1</b>	<b>9924</b>	<b>34.0%</b>	<b>10848</b>	<b>3329</b>	<b>23.3%</b>	<b>3.3</b>		<b>67.4</b>
Single	Nerve Block	86	40	2.2	10	11.6%	50	21	29.2%	2.4	16	28.3
	Sacroiliac	963	489	2.0	127	13.2%	494	390	47.8%	1.3	28	51.0
<b>Total Single</b>		<b>1049</b>	<b>529</b>	<b>2.0</b>	<b>137</b>	<b>13.1%</b>	<b>544</b>	<b>411</b>	<b>46.3%</b>	<b>1.3</b>		<b>48.9</b>
<b>Grand Total</b>		<b>35530</b>	<b>9098</b>	<b>3.9</b>	<b>11861</b>	<b>33.4%</b>	<b>12960</b>	<b>4202</b>	<b>23.8%</b>	<b>3.1</b>		<b>65.3</b>

**Figure 5b: DLI Spinal Injection Repeat Procedure Table, 2006-2009**

*NOTE: Table modified 2/25/2011 due to miscounts of members with multiple procedures on different days – members with multiple procedures of different types were counted under the category of the final procedure, requiring corrections to both procedure and member counts - Columns modified: 4, 8-13*

Injection		Average procedure count per member			Same day multiple Procs		Different day repeated procedures					
Level	Type	Proc ct	Mbr ct	Average	Proc ct	% Procs	Proc day repeats	Mbr ct	% Mbrs	Avg Proc Days/ Mbr	Max Procs/ Mbr	Avg days between procs
C/T	Epidural	3978	1488	2.7	2457	61.80%	1709	657	44.15%	2.6	9	84.6
	Foraminal	3594	957	3.8	2350	65.40%	1312	474	49.53%	2.8	8	97.2
	Paravertebral	7121	1120	6.4	5874	82.50%	1219	470	41.96%	2.6	7	92.7
<b>Total C/T</b>		<b>14693</b>	<b>3565</b>	<b>4.1</b>	<b>10681</b>	<b>72.70%</b>	<b>4240</b>	<b>1601</b>	<b>44.91%</b>	<b>2.6</b>		<b>91.0</b>
L/S	Epidural	13845	5185	2.7	8480	61.20%	6124	2390	46.09%	2.6	11	81.6
	Foraminal	27273	3217	8.5	19179	70.30%	4020	1503	46.72%	2.7	8	86.7
	Paravertebral	25110	6550	3.8	22100	88.00%	9825	3516	53.68%	2.8	15	87.1
<b>Total L/S</b>	<b>Single Level</b>	<b>66228</b>	<b>14952</b>	<b>4.4</b>	<b>49759</b>	<b>75.10%</b>	<b>19969</b>	<b>7409</b>	<b>49.55%</b>	<b>2.7</b>		<b>85.4</b>
<b>Single</b>	Nerve Block	1642	258	6.4	1387	84.50%	547	156	60.47%	3.5	14	44.7
	Sacroiliac	3608	1163	3.1	2690	74.60%	995	345	29.66%	2.9	31	67.2
	<b>Total Single</b>	<b>5250</b>	<b>1421</b>	<b>3.7</b>	<b>4077</b>	<b>77.70%</b>	<b>1542</b>	<b>501</b>	<b>35.26%</b>	<b>3.1</b>		<b>58.7</b>
<b>Grand Total</b>		<b>86171</b>	<b>19938</b>	<b>4.3</b>	<b>64517</b>	<b>74.90%</b>	<b>25751</b>	<b>9511</b>	<b>47.70%</b>	<b>2.7</b>		<b>84.6</b>

*\*DLI repeated procedures were calculated using Claimant ID rather than claim number.*

**Figure 5c DSHS Spinal Injection Repeat Procedure Table, 2006-2009**

*NOTE: Table modified 2/25/2011 due to miscounts of members with multiple procedures on different days – members with multiple procedures of different types were counted under the category of the final procedure, requiring corrections to both procedure and member counts - Columns modified: 8-13*

Injection		Average procedure count per member			Same day multiple Procs		Different day repeated procedures					
Level	Type	Proc ct	Mbr ct	Avg	Proc ct	% Procs	Proc ct	Mbr ct	% Mbrs	Avg Procs/ Mbr	Max Procs/ Mbr	Avg days between procs
<b>C/T</b>												
	Epidural	2403	979	2.5	1351	56.22%	1131	381	38.92%	3.0	14	72.0
	Foraminal	507	221	2.3	331	65.29%	173	54	24.43%	3.2	26	51.7
	Paravertebral	1788	430	4.2	1546	86.47%	436	152	35.35%	2.9	15	70.9
<b>Total C/T</b>		<b>4698</b>	<b>1630</b>	<b>2.9</b>	<b>3228</b>	<b>68.71%</b>	<b>1737</b>	<b>587</b>	<b>36.01%</b>	<b>3.0</b>		<b>69.8</b>
<b>L/S</b>												
	Epidural	9308	3648	2.6	5089	54.67%	4671	1585	43.45%	2.9	20	68.2
	Foraminal	9235	2698	3.4	6935	75.09%	3534	1132	41.96%	3.1	18	80.9
	Paravertebral	6352	1458	4.4	5658	89.07%	1530	554	38.00%	2.8	31	68.3
<b>Total L/S</b>		<b>24895</b>	<b>7804</b>	<b>3.2</b>	<b>17682</b>	<b>71.03%</b>	<b>9735</b>	<b>3271</b>	<b>41.91%</b>	<b>3.0</b>		<b>72.8</b>
<b>Single</b>												
	Nerve Block	91	41	2.2	23	25.27%	50	16	39.02%	3.1	5	78.1
	Sacroiliac	702	435	1.6	120	17.09%	328	124	28.51%	2.6	18	79.7
<b>Total Single</b>		<b>793</b>	<b>476</b>	<b>1.7</b>	<b>143</b>	<b>18.03%</b>	<b>378</b>	<b>140</b>	<b>29.41%</b>	<b>2.7</b>		<b>79.5</b>
<b>Grand Total</b>		<b>30376</b>	<b>9910</b>	<b>3.1</b>	<b>21053</b>	<b>69.31%</b>	<b>11850</b>	<b>3998</b>	<b>40.34%</b>	<b>2.963982</b>		<b>72.6</b>

Figure 6a: UMP/PEP Spinal Injection Procedure Direct Costs and Counts by Age Group, 2006-2009

UMP/PEP	Procedure Costs				Procedure Counts				Totals	
Age Group	2006	2007	2008	2009	2006	2007	2008	2009	4 Yr Cost	4 yr Cnt
0-18	\$5,167	\$5,076	\$16,737	\$4,582	33	22	37	30	\$31,563	122
19-35	\$76,840	\$95,264	\$145,828	\$183,900	226	260	374	501	\$501,832	1361
36-50	\$330,076	\$305,191	\$561,864	\$641,154	1000	959	1661	1816	\$1,838,284	5436
51-65	\$774,112	\$941,763	\$1,171,655	\$1,373,829	2517	3007	3787	4484	\$4,261,359	13795
>65	\$199,593	\$230,571	\$277,955	\$310,853	3039	3338	3899	4540	\$1,018,972	14816
<b>Grand Total</b>	<b>\$1,385,787</b>	<b>\$1,577,866</b>	<b>\$2,174,039</b>	<b>\$2,514,318</b>	<b>6815</b>	<b>7586</b>	<b>9758</b>	<b>11371</b>	<b>\$7,652,010</b>	<b>35530</b>

Figure 6b: DLI Spinal Injection Procedure Direct Costs and Counts by Age Group, 2006-2009

DLI	Procedure Costs				Procedure Counts				Totals	
Age Group	2006	2007	2008	2009	2006	2007	2008	2009	4 Yr Cost	4 yr Cnt
0-18	\$25,158	\$21,406	\$14,646	\$8,834	56	62	38	24	\$70,044	180
19-35	\$1,625,957	\$1,525,191	\$1,769,561	\$1,832,397	3946	3893	4391	5295	\$6,753,107	17525
36-50	\$4,234,308	\$3,924,361	\$4,031,715	\$3,883,955	10872	9819	10757	11406	\$16,074,338	42854
51-65	\$1,882,036	\$2,258,669	\$2,289,940	\$2,452,770	5074	5583	6577	7015	\$8,883,415	24249
>65	\$94,630	\$135,303	\$114,048	\$119,636	260	357	354	392	\$463,617	1363
<b>Grand Total</b>	<b>\$7,862,089</b>	<b>\$7,864,930</b>	<b>\$8,219,911</b>	<b>\$8,297,592</b>	<b>20208</b>	<b>19714</b>	<b>22117</b>	<b>24132</b>	<b>\$32,244,521</b>	<b>86171</b>

Figure 6c: DSHS Procedure Spinal Injection Direct Costs and Counts by Age Group, 2006-2009

DSHS	Procedure Costs				Procedure Counts				Totals	
Age Group	2006	2007	2008	2009	2006	2007	2008	2009	4 Yr Cost	4 yr Cnt
0-18	\$691	\$2,191	\$1,544	\$2,649	5	14	10	15	\$7,075	44
19-35	\$108,317	\$95,732	\$122,040	\$149,962	686	553	708	849	\$476,051	2796
36-50	\$542,028	\$517,975	\$577,223	\$658,595	3360	2954	3371	3773	\$2,295,821	13458
51-65	\$438,102	\$465,596	\$485,544	\$572,959	2771	2712	3054	3446	\$1,962,201	11983
>65	\$37,247	\$33,424	<b>\$60,414</b>	\$37,942	453	461	649	542	\$169,026	2105
<b>Grand Total</b>	<b>\$1,126,385</b>	<b>\$1,114,918</b>	<b>\$1,246,765</b>	<b>\$1,422,107</b>	<b>7275</b>	<b>6694</b>	<b>7792</b>	<b>8625</b>	<b>\$4,910,174</b>	<b>30386</b>

Related Medical Codes			
Code Type	Codes	Short Description	Additional Info
Procedure Codes			
Sacroiliac joint injection	27096	Injection procedure for sacroiliac joint	Anes/Steroid
Epidural Injections to the Spine	62310	INJECT SPINE Cervical/Thoracic	Anes/Anti spasm/ opioid or steroid inj
	62311	INJECT SPINE Lumbar/Sacral	Anes/Anti spasm/ opioid or steroid inj
Facet/ Paravertebral/ Medial Branch Block	64470	DEL - INJ PARAVERTEBRAL C/T 1/2010 del	Anes or Steroid
	64472	DEL - INJ PARAVERTEBRAL C/T ADD-ON 1/2010 del	
	64475	DEL - INJ PARAVERTEBRAL L/S 1/2010 del	
	64476	DEL - INJ PARAVERTEBRAL L/S ADD-ON 1/2010 del	
	64479	INJ FORAMEN EPIDURAL C/T	
	64480	INJ FORAMEN EPIDURAL ADD-ON	
	64483	INJ FORAMEN EPIDURAL L/S	
	64484	INJ FORAMEN EPIDURAL ADD-ON	
Nerve Block	64520	N BLOCK, LUMBAR/THORACIC	Anes
Guidance and Imaging – additl codes	72275	EPIDUROGRAPHY	
	76005	DEL - FLUOROGUIDE FOR SPINE INJECT	
	77003	FLUOROGUIDE FOR SPINE INJECT	
Future Analysis	64490-64495	New paravertebral facet joint or associated nerves w/wo image guidance (2010)	
	0216T/0217T/0218T	0216T Injection(s), diagnostic or therapeutic agent, paravertebral facet (zygapophyseal) joint (or nerves innervating that joint) with ultrasound guidance, lumbar or sacral; single level (2 <sup>nd</sup> level, 3 <sup>rd</sup> level <a href="http://www.ama-assn.org/ama1/pub/upload/mm/362/cptcat3codes.pdf">http://www.ama-assn.org/ama1/pub/upload/mm/362/cptcat3codes.pdf</a>	1/2010
ICD-9 Procedure Codes	03.91	Injection of anesthetic into spinal canal for analgesia	
	03.92	Injection of another agent into spinal canal	

Related Medical Codes, cont.			
Code Type	Codes	Short Description	Additional Info
Diagnosis Codes			
ICD-9 Diagnosis	053	Neuropathies, various	
	337	Sympathetic dystrophies, various	
	340	Multiple sclerosis	
	353	Nerve root lesions, various	
	354-355	Neuritis and causalgia, various	
	720.9	Unspecified inflammatory spondylopathy	
	721	Spondylosis , various	
	722	Degeneration/displacement intervertebral disc, various	
	723	Spinal stenosis, brachial neuritis or radiculitis, various	
	724	Spinal stenosis, various	
	733.13	Vertebral compression fracture	
	737.30	Scoliosis/kyphoscoliosis, idiopathic	
	738.4	Acquired spondylolisthesis	
	805	Closed vertebral fractures, various	
	847.0	Strain/sprain, cervical	
	847.2	Strain/sprain, lumbar	
	953	Nerve root injuries, various	

#### 4.4.2. Description of included studies

**PRICE 2005 (NHS HTA)<sup>164</sup>:** As part of a health technology assessment conducted for the UK National Institute for Clinical Effectiveness (NICE), a cost utility analysis was conducted based on trial data from one pragmatic multisite randomized controlled trial (Arden et al (2005)<sup>7</sup>). The trial compared one to three epidural steroid injections to placebo saline injections in adults with acute or chronic sciatica. Outcomes assessed were function (Oswestry Disability Questionnaire), pain, and quality of life (SF-36). The number needed to treat (NNT), costs, and incremental cost effectiveness ratios (ICER) were calculated from a purchaser perspective (all charges plus overhead) and for two scenarios: trial protocol (up to three injections) and one epidural steroid injection only. One-way sensitivity analyses of study variables were conducted.

The RCT reported an early benefit (three weeks) in pain relief following epidural steroid injection compared to placebo, but by six weeks and until the end of study follow-up (twelve months) the two arms were equivalent for pain and all other outcomes. There was no additional benefit to more than one injection. Based on the results, the authors recommend a

management strategy of only one injection. The total benefit of epidural steroid injections was estimated at 2.2 days of full health (NNT = 11.4). Cost per patient for the trial protocol of up to three injections was £2102, and £992 based on a management strategy of only one injection. The incremental cost effectiveness ratio of one injection from the purchaser perspective was £354,171/QALY (quality-adjusted life years) for the trial protocol of up to three injections and £167,145/QALY for only one injection. The authors concluded that the cost effectiveness ratios are higher than the implied thresholds used by NICE and therefore do not support coverage by the NHS. Further, given the high frequency with which epidural steroid injections are used in the NHS, a strategy of only one epidural steroid injection per patient would save the NHS £31 million.

This is a reasonably well conducted study (QHES score = 78/100). Its strengths are in its use of clinical trial data and in its calculation of cost effectiveness estimates from a purchaser perspective. Given the small, transient benefit of ESI in the trial, it is logical that cost effectiveness ratios would be relatively high, even for a moderately priced intervention.

**KARPPINEN 2001<sup>94, 95</sup>:** In this trial the authors collected costs alongside a double-blind randomized controlled trial of epidural steroid injection versus saline injection in 160 sciatica patients. Outcomes assessed were pain, function (Oswestry Disability Questionnaire), and duration of sick leave. Costs were estimated from the trial and medical records and study questionnaires using the Finnish national insurance registry, as well as the cost of home help. Sick leave was not valued. Cost per patient was calculated for the main two study groups as well as subgroups of MRI-based classification of bulge, contained herniation, or extrusion.

The results of the trial<sup>94</sup> indicated that by one year there were no statistically significant differences in either costs or outcomes. However, there was early benefit (at four weeks) in leg pain, leg function, and patient satisfaction favoring ESI. By three and six months, back and leg pain, respectively, were significantly lower in the saline group. In terms of cost, the epidural steroid injection group had fewer therapy visits and medication costs at four weeks; all other costs were similar and by one year there were no significant cost differences between the groups. Sick leaves and medical costs were similar in both groups. The authors conclude that epidural steroid injections produced cost savings at four weeks in medication and therapy costs but that by one year overall costs were similar. A subgroup analysis of MRI classification suggested that cost per “responder” (75% or more leg pain reduction) favors injection only in contained hernias (\$4432 versus \$17,098,  $P = 0.0073$ ), while bulges were similar (\$3740 versus \$3629, NS) and extrusions favored saline injection (\$7165 versus \$2484,  $P = 0.0058$ )<sup>95</sup>. The authors suggest that these subgroup findings should be verified.

This is a relatively poorly conducted economic evaluation (QHES rating: 49/100), with the lack of sensitivity analysis, long-term modeling, and statement of perspective as major limitations. However, a main strength of this study is that it provides real patient-level data from a randomized trial. The time horizon included (one year), relatively short term from an economic standpoint, suggests that over time the costs of ESI are similar to those in a saline injection group, but that stratifying future work according to MRI classification may be warranted.

## Summary

***Lumbar epidural steroid injections:*** There is no evidence that epidural steroid injections are cost effective.

- One moderately well conducted cost utility analysis suggested that one epidural steroid injection is a more cost effective than up to three injections; however, the cost effectiveness ratios for even one epidural steroid injection are too high to be considered cost effective by UK conventions. Further, the budget impact of epidural spinal injections is likely large because of high use.
- Poor economic data from one trial (Karppinen) suggested that over one year epidural steroid injections do not show cost or outcome advantages compared to saline injections, and that contained herniations may be more responsive to steroid injection than bulges or extrusions.

***Lumbar facet joint injections, medial branch blocks, sacroiliac joint injections, intradiscal injections:***

- No economic data were available for facet injections, medial branch blocks, sacroiliac joint injections, or intradiscal injections.

***Cervical spinal injections:***

- No economic data were available for any type of cervical spinal injections.

**Overall, evidence to assess the economic considerations of spinal injections is very low.**

In order to adequately assess the cost effectiveness of spinal injections, long term studies (beyond one year) of the clinical effectiveness of spinal injections, including adverse events and subsequent medical care and economic evaluations of facet injections, medial branch blocks, sacroiliac joint injections, or intradiscal injections would be required.

## 5. Summary and Implications

### Results/Summary

**Table 23. Summary of evidence for Key Question 1.**

Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?						
Indication	Comparator	SoE	Conclusions/Comments	Quality	Quantity	Consistency
<b>Lumbar caudal or interlaminar epidural steroid injections:</b>						
<ul style="list-style-type: none"> <li>low back pain with sciatica or radiculopathy</li> </ul>	placebo	<b>Low*</b>	<ul style="list-style-type: none"> <li><u>In the short-term</u> (<math>\leq 3</math> months) there was <b>mixed evidence</b> based on data from twenty RCTs, seventeen of which were included in the Chou/APS SR<sup>39, 40</sup> (seven were considered to be higher-quality trials). Seven of seventeen studies included in the SR reported no benefit or inferior results while another seven reported positive results and three reported unclear results. Three LoE IIb RCTs published after the SR were added here, two reported on pain (both negative) and three on function (two negative and one positive) at three months.</li> <li><u>In the long-term</u> (<math>&gt; 3</math> months) there was <b>mixed evidence</b> based on data from twelve RCTs, nine of which were included in the Chou/APS SR<sup>39, 40</sup>. Seven of nine studies included in the SR reported no benefit or inferior results while positive results were reported by one study and another reported mixed results. Regarding the more recent RCTs included here, two reported on pain (both negative at twelve months, although one was positive at six months) and three on function (mixed results, one positive, one mixed, and one negative).</li> </ul>	+	+	-

Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?						
Indication	Comparator	SoE	Conclusions/Comments	Quality	Quantity	Consistency
<ul style="list-style-type: none"> <li>low back pain <u>without</u> sciatica or radiculopathy</li> </ul>	placebo	<b>Moderate*</b>	<ul style="list-style-type: none"> <li><b>no benefit</b> based on data from three RCTs, one of which was included in the Chou/APS SR and considered to be a lower-quality trial<sup>39, 40</sup>. In the two recent LoE IIb RCTs included here, there was no benefit in pain, function, or opioid use at three or in employment at twelve months.</li> </ul>	+	+	+
<ul style="list-style-type: none"> <li>spinal stenosis</li> </ul>	placebo	<b>Low* to moderate*</b>	<ul style="list-style-type: none"> <li><u>In the short-term</u> (24 hours – 3 months), there was <b>no benefit</b> based on data from four RCTs, three of which was included in the Chou/APS SR; one was considered to be a higher-quality trial<sup>39, 40</sup>. Three of four studies reported no benefit; one study reported improved walking distance at one week. In the one recent LoE IIb RCT included here, there was no benefit in pain, function, or opioid use at three months. (<b>SoE = moderate</b>)</li> <li><u>In the long-term</u> (13 – 30 months), there was <b>no benefit</b> based on data from two RCTs as reported in the Chou/APS SR<sup>39, 40</sup>. (<b>SoE = low</b>)</li> </ul>	+	+/-	+
<ul style="list-style-type: none"> <li>failed back surgery syndrome</li> </ul>	placebo	<b>Moderate*</b>	<ul style="list-style-type: none"> <li><b>no benefit</b> based on data from three RCTs, two of which were included in the Chou/APS SR and considered to be lower-quality trials<sup>39, 40</sup>. In the one recent LoE IIb RCT included here, there was no benefit in pain, function, or opioid use at three months.</li> </ul>	+	+	+

Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?						
Indication	Comparator	SoE	Conclusions/Comments	Quality	Quantity	Consistency
• various	adhesiolysis	Low <sup>†</sup>	• <b>no benefit</b> based on data from five RCTs, three of which were included in the Chou/APS SR (one was considered higher-quality but with limitations) <sup>39, 40</sup> . In the two recent LoE IIb RCTs included here, there was no benefit in pain, function, or opioid use at three months. One study reported no benefit at twelve months as reported in the Chou/APS SR <sup>39, 40</sup> . <b>However</b> , three of the studies only enrolled patients who had who had previously failed epidural injections, and epidural injections served as the control, not as the intervention.	+	+	+
• spinal stenosis	physical therapy or control	Very low*	• <b>no benefit</b> in terms of pain, function, or quality of life at three and six months based on data from one LoE IIb RCT.	+	-	NA
• sciatica and radiculopathy	trigger point injection	Low	• <b>In the short-term, epidural steroid injections were “modestly” superior</b> at three months based on data from one higher-quality RCT as reported in the Chou/APS SR <sup>39, 40</sup> . No long-term data were reported.	+	-	NA
• sciatica	dry needling of the interspinous ligament	Very low*	• <b>no benefit</b> based on data from one lower-quality RCT as reported in the Chou/APS SR <sup>39, 40</sup> . The length of follow-up was not reported.	+	-	NA
• low back pain with sciatica	intramuscular steroid injections	Low	• <b>no benefit</b> at two years based on data from one higher-quality RCT as reported in the Chou/APS SR <sup>39, 40</sup> . No short-term data were reported.	+	-	NA
• disc prolapse	discectomy	Low	• <b>no benefit (inferior)</b> in the short-term and up to two to three years based on data from one higher-quality RCT as reported in the Chou/APS SR <sup>39, 40</sup> .	+	-	NA

Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?						
Indication	Comparator	SoE	Conclusions/Comments	Quality	Quantity	Consistency
<b>Lumbar transforaminal epidural steroid injections:</b>						
• low back pain <u>with</u> sciatica or radiculopathy	placebo	<b>Low*</b>	• <b>mixed evidence</b> based on data from four RCTs, two of which were included in the Chou/APS SR and considered to be higher-quality <sup>39, 40</sup> and two of which were more recent LoE IIb studies. In terms of pain relief, the data suggest a benefit at two weeks (one study), mixed results at one month (two studies- one positive and one negative), and no benefit by 3 months. No benefit in function was reported at three months by two studies. Long-term data were mixed as reported by two higher-quality RCTs, both of which were reported in the Chou/APS SR <sup>39, 40</sup> , with one study reported positive results while the other showed no benefit.	+	+/-	-
• low back pain <u>with</u> sciatica or radiculopathy	intramuscular injection	<b>Low</b>	• <b>transforaminal steroid injections were superior to intramuscular injections</b> in terms of pain relief at one month based on data from one LoE IIb RCT.	+	-	NA
• disc prolapse	oxygen-ozone ± steroids	<b>Low*</b>	• <b>no benefit</b> with no difference or inferior results at one week, three months, and six months based on data from two lower-quality RCTs as reported in the Chou/APS SR <sup>39, 40</sup> .	+	-	+
<b>Lumbar intraarticular facet joint steroid injections:</b>						
• confirmed or presumed facet joint pain	placebo	<b>Low*</b>	• <b>no benefit</b> in the first three months based on data from two RCTs included in the Chou/APS SR, one of which was considered to be lower-quality <sup>39, 40</sup> . Although one of the studies reported a statistically meaningful benefit at six months in patient improvement following steroid	+	-	+

Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?						
Indication	Comparator	SoE	Conclusions/Comments	Quality	Quantity	Consistency
			injection, the rationale for this late response is not clear.			
• presumed facet joint pain	home stretching	<b>Very low*</b>	• <b>no benefit</b> in facet joint injections plus home stretching versus home stretching alone based on data from one lower-quality RCT included in the Chou/APS SR <sup>39, 40</sup> .	+	-	NA
• non-radicular back pain and facet joint osteoarthritis	facet injections with hyaluronic acid	<b>Low</b>	• <b>no benefit</b> in the injection of steroids versus hyaluronic acid into the facet joint at six months based on data from one higher-quality RCT included in the Chou/APS SR <sup>39, 40</sup> .	+	-	NA
<b>Lumbar medial branch blocks:</b>						
• confirmed facet joint pain	placebo	<b>Very low*</b>	• <b>no benefit</b> in terms of pain or function at both three and twelve months or on opioid use at twelve months based on data from one LoE IIb RCT.	+	-	NA
• presumed facet joint pain	Sarapin	<b>Low*</b>	• <b>no benefit</b> in injections with Sarapin with or without steroid based on data from one higher-quality and one lower-quality RCT included in the Chou/APS SR <sup>39, 40</sup> .	+	-	+
<b>Lumbar sacroiliac joint steroid injections:</b>						
• sacroiliac joint pain	placebo	<b>Low</b>	• <b>sacroiliac joint injections were superior</b> to placebo injections based on data from one higher-quality RCT included in the Chou/APS SR <sup>39, 40</sup> .	+	-	NA
<b>Lumbar intradiscal steroid injections:</b>						
• discogenic back pain	placebo	<b>Moderate*</b>	• <b>no benefit</b> based on data from three RCTs included in the Chou/APS SR, one of which was higher-quality <sup>39, 40</sup> .	+	+	+
• sciatica	chemo-nucleolysis	<b>Moderate*</b>	• <b>no benefit</b> based on data from three RCTs included in the Chou/APS SR, one of which was	+	+	+

Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?						
Indication	Comparator	SoE	Conclusions/Comments	Quality	Quantity	Consistency
			higher-quality <sup>39, 40</sup> .			
			•			
<b>Lumbar intradiscal injections with neurolytic agent:</b>						
• low back pain without radiculopathy	placebo	Low	• <b>intradiscal injections with methylene blue were superior</b> to placebo injections in terms of pain, function, patient satisfaction, and analgesic use in the long-term (6-24 months) based on data from one LoE IIa RCT.	+	-	NA
<b>Cervical epidural steroid injections:</b>						
• neck pain with disc herniation and radiculitis	placebo	Very low*	• <b>no benefit</b> in terms of pain, function, or opioid use at both three and twelve months or on employment at twelve months based on data from one LoE IIb RCT.	+	-	NA
• neck pain <u>without</u> disc herniation and radiculitis	placebo	Very low*	• <b>no benefit</b> in terms of pain, function, or opioid use at both three and twelve months or on employment at twelve months based on data from one LoE IIb RCT.	+	-	NA
• neck pain with disc compression and radiculitis	intramuscular injection	Very low*	• <b>epidural injections were superior</b> to intramuscular injections in the posterior neck in terms of pain, analgesic use, and employment at one week and twelve months based on data from one LoE IIb RCT.	+	-	NA
<b>Cervical intraarticular facet joint steroid injections:</b>						
• confirmed facet joint pain	placebo	Very low*	• <b>no benefit</b> in terms of the length of pain relief based on data from one LoE IIb RCT. No long-term data was reported.	+	-	NA
<b>Cervical medial branch blocks:</b>						
• confirmed facet joint pain	placebo	Very low*	• <b>no benefit</b> in terms of pain or function at both three and twelve months or on opioid use or employment at twelve months based on data from one LoE IIb	+	-	NA

Key Question 1: What is the evidence of efficacy and effectiveness of spinal injections?						
Indication	Comparator	SoE	Conclusions/Comments	Quality	Quantity	Consistency
			RCT.			

NA: not applicable

\* Overall strength of evidence rating was downgraded one level due to limitations in study design or execution.

† Overall strength of evidence rating was downgraded two levels as at least two of the three trials had serious limitations in their design: inclusion criteria limited enrollment to patients who had who had previously failed epidural injections, and epidural injections served as the control treatment.

**Table 24. Summary of evidence for Key Question 2.**

Key Question 2: What is the evidence of the safety of spinal injections?					
Spinal injections	Strength of evidence	Conclusions/Comments	Quality	Quantity	Consistency

<ul style="list-style-type: none"> <li>Major complications</li> </ul>	<p><b>High</b></p>	<ul style="list-style-type: none"> <li><b>Major complications are rare</b> following injections into the lumbar or cervical spine. There were no cases of death or paralysis in the included studies, although there have been case reports of each in the published literature.</li> <li><b>Lumbar injections:</b> In 14 recent RCTs, there were reports of dural puncture, subarachnoid puncture, and angina pectoris in 1/1556 injections or patients (each). In six case series there was one case each of dural puncture and subarachnoid puncture (1/10,416 injections or patients (each)). No deaths were attributed to spinal injection procedures; death unrelated to the procedure occurred in 10/1146 patients in the RCTs. Chou reported in the APS SR<sup>39, 40</sup> that major complications were rare but inadequately reported in trials of lumbar epidural steroid injections, and noted one case of dural puncture.</li> <li><b>Cervical injections:</b> In five RCTs, there were reports of subarachnoid puncture in 3/710 injections or patients and no reports of dural puncture or death. In four case series there were reports of life-threatening generalized anaphylactic reaction (1 case), grand-mal seizure (1 case), dural puncture (2 cases), and local hematoma (1 case) in 7240 injections or patients.</li> </ul> <p>In three case reports of a <u>mix of lumbar and cervical spinal injection patients</u>, there was one case of each of the following major complications in 6935 injections: chest pain, tachycardia/hypertension, significant transient hypertensive episode, hematoma, dural puncture, and a severe vasovagal reaction.</p>	<p>+</p>	<p>+</p>	<p>+</p>
<ul style="list-style-type: none"> <li>Minor complications</li> </ul>	<p><b>High</b></p>	<ul style="list-style-type: none"> <li><b>Minor complications are more common but are generally transient in nature.</b> The overall minor complication rate ranged from 0.06% to 16.3% of injections or patients in 19 RCTs and 14 case series, and complications included: pain at the injection site, increased radicular pain/numbness/weakness, nerve root irritation, superficial infections, sympathetic blockade, facial flushing, vasovagal reactions/fainting, headache, gastric complaints, dizziness, pruritis, irregular periods, and insomnia.</li> </ul>	<p>+</p>	<p>+</p>	<p>+</p>

<ul style="list-style-type: none"> <li>• Vascular puncture</li> </ul>	<p><b>Low</b></p>	<ul style="list-style-type: none"> <li>• <b>The mean incidence of intravascular puncture following fluoroscopically guided lumbar spinal injections was 10.18%</b> (range, 1.9–22%) as reported in five case series designed to assess its incidence. These studies evaluated the incidence but not the consequences of intravascular injection.</li> </ul>	-	+	+
<ul style="list-style-type: none"> <li>• Radiation exposure to the physician</li> </ul>	<p><b>Low</b></p>	<ul style="list-style-type: none"> <li>• <b>With proper protective measures, total radiation exposure was within normal limits</b> following a mean of 923 procedures (range, 100 – 1819) with an average length of radiation exposure of 9.8 seconds/procedure (range, 4.9 – 15.2) in all five case series we identified.</li> </ul>	-	+	+

**Table 25. Summary of evidence for Key Question 3.**

<b>Key Question 3: What is the evidence that spinal injections have differential efficacy or safety issues in sub populations?</b>					
<b>Spinal injections</b>	<b>Strength of evidence</b>	<b>Conclusions/Comments</b>	<b>Quality</b>	<b>Quantity</b>	<b>Consistency</b>
<b>Epidural Steroid Injection</b>					
• Approach of epidural steroid injection	<b>Low*</b>	• There is <b>no consistent evidence</b> from a systematic review of six RCTs and two additional RCTs published since the systematic review that one approach is more efficacious in administering lumbar epidural steroid. The results of one lower quality RCT suggest that interlaminar injections may not be as efficacious as transforaminal in patients with axial only pain from spinal stenosis. However, more study is needed to verify these findings.	+	+	–
• Diagnosis	<b>Very low</b>	• There is <b>no consistent evidence</b> that epidural steroid injections have differential efficacy or effectiveness among various diagnoses of the lumbar or cervical spine.	–	+	–
• Pre-injection pain intensity or duration, type of steroid, sex, age, or MRI findings	<b>Very low</b>	• There is <b>no consistent evidence</b> that pre-injection pain intensity or duration, type of steroid used as injectate, sex, age or pre-injection MRI findings are associated with outcome in patients receiving epidural steroid injections of the lumbar or cervical spine.	–	+	–

NA: not applicable

\* Overall strength of evidence rating was downgraded one level due to limitations in study design or execution.

**Table 26. Summary of evidence for Key Question 4.**

Key Question 4: What is the evidence of cost implications and cost-effectiveness of spinal injections?					
	Strength of evidence	Conclusions/Comments	Quality	Quantity	Consistency
<ul style="list-style-type: none"> <li>Economic analysis</li> </ul>	Very low	<ul style="list-style-type: none"> <li><b>There is no evidence that epidural steroid injections are cost effective</b> based on data from two economic analyses. One moderately well conducted cost utility analysis (QHEs 78/100) suggested that one epidural steroid injection is a more cost effective patient management strategy than up to three injections and that cost effectiveness ratios for epidural steroid injections are too high to be considered cost effective by UK conventions. Further, the budget impact of epidural spinal injections is likely large because of high use. Poor economic data (QHEs 49/100) from a second trial (Karppinen) suggested that over one year epidural steroid injections do not show cost or outcome advantages compared to saline injections, and that contained herniations may be more responsive to steroid injection than bulges or extrusions.</li> <li>No economic data were available for facet injections, medial branch blocks, sacroiliac joint injections, or intradiscal injections or for any type of cervical injection.</li> </ul>	—	—	—

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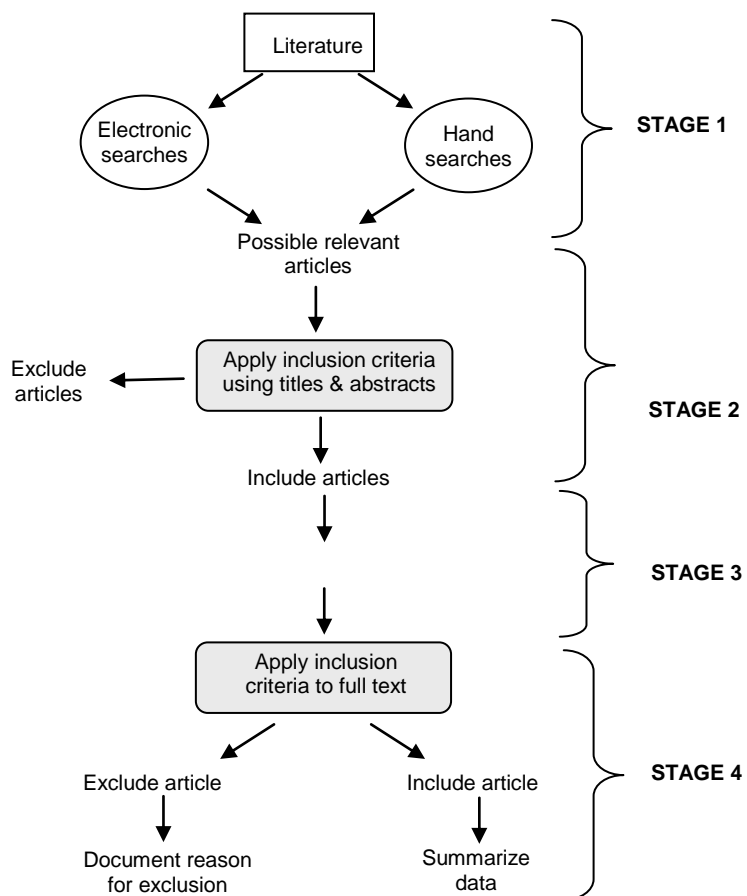
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## Appendix A. ALGORITHM FOR ARTICLE SELECTION



## Appendix B. SEARCH STRATEGIES

Database: MEDLINE

Limit: English

1.	“Injections, Spinal”[MESH]	10,085
2.	Injection*	448,700
3.	Epidural OR facet OR sacroiliac OR intradiscal	34,438
4.	#2 AND #3	5163
5.	“medial branch”	281
6.	#4 OR #5	5392
7.	#1 AND #6	2157
8.	Pain	352,335
9.	Back OR neck OR spinal OR cervical OR lumbar OR sacral	537,833
10.	#8 AND #9	69,424
11.	#7 AND #10	1018
12.	#11 NOT(In Vitro[Publication Type] OR Cadaver*[tw] OR Case Reports[Publication Type] OR Infant[mh] OR Child[mh] OR Adolescent[mh] OR rat[tw] OR rats[tw] OR mouse[tw] OR mice[tw] OR dog[tw] or dogs[tw])	677

**OR**

**Limit: English**

1.	Spine[mh] OR Spinal Nerve Roots[mh]	86,137
2.	spine[tw] OR spinal[tw] OR back[tw] OR coccyx[tw] OR intervertebral disk[tw] OR lumbar vertebrae[tw] OR cervical vertebrae[tw] OR sacral[tw] OR sacrum[tw] OR spinal canal[tw] OR facet joint[tw] OR sacroiliac[tw] OR intradisc*[tw]	338,623
3.	#1 OR #2	341,398
4.	Injection*[tw] OR Injections, Spinal[mh]	449,042
5.	“medial branch block*”[tw]	19
6.	(Spine*[tw] or spinal*[tw] or nerv*[tw]) AND block*[tw]	64,887
7.	Anesthesia, Conduction[mh]	33,577
8.	Anesthetics[mh] OR Anti-Inflammatory Agents[mh]	132,872
9.	#4 OR #5 OR #6 OR #7 OR #8	632,739
10.	#9 NOT (extraspinal[tw] or Botulinum[tw] OR prolotherap*[tw] OR chemonucleolysis[tw] or chemonucleolysis[mh] OR radiofrequency denerv*[tw] OR intradiscal electrothermal*[tw] OR coblation[tw])	627,815
11.	Spinal Diseases[mh] OR Peripheral Nervous System Diseases[mh]	124,181
12.	Spinal disease*[tw] OR hyperostosis[tw] OR spinal stenosis[tw] OR intervertebral disk displacement[tw] OR spinal osteophytosis[tw] OR hyperostosis[tw] OR diffuse idiopathic	31,588

	skeletal[tw] OR Sciatica[tw] OR radicul*[tw]	
13.	Back Pain[mh] OR Neck Pain[mh] OR Back Pain[tw]	24,812
14.	#11 OR #12 OR #13	150,069
15.	#14 NOT (Nervous System Neoplasms[mh] OR Spinal Neoplasms[mh] OR Neoplasms[mh] OR Labor, Obstetric[mh] OR labor[tw] OR labour[tw] OR cauda equina syndrome*[tw] OR fibromyalg*[tw] OR spondylo*[tw] OR spondyliti*[tw] OR vertebral compression fracture*[tw] OR osteoporosis*[mh] OR Osteoporosis[mh])	104,454
14.	#3 AND #10 AND #15	4583
15.	#14 NOT(In Vitro[Publication Type] OR Cadaver*[tw] OR Case Reports[Publication Type] OR Infant[mh] OR Child[mh] OR Adolescent[mh] OR rat[tw] OR rats[tw] OR mouse[tw] OR mice[tw] OR dog[tw] or dogs[tw])	2352

Parallel strategies were used to search the Cochrane Library and others listed below. Keyword searches were conducted in the other listed resources.

### ***Electronic Database Searches***

The following databases have been searched for relevant information (through August, 2010):

Agency for Healthcare Research and Quality (AHRQ)

Cumulative Index to Nursing and Allied Health (CINAHL)

Cochrane Database of Systematic Reviews

Cochrane Registry of Clinical Trials (CENTRAL)

Cochrane Review Methodology Database

Computer Retrieval of Information on Scientific Projects(CRISP)

Database of Reviews of Effectiveness (Cochrane Library)

EMBASE (1985 through August, 2010)

PubMed (1975 through August, 2010)

Informational Network of Agencies for Health Technology Assessment(INAHTA)

NHS Economic Evaluation Database

HSTAT(Health Services/Technology Assessment Text)

EconLIT

### ***Additional Economics, Clinical Guideline and Gray Literature Databases***

AHRQ- Healthcare Cost and Utilization Project

Canadian Agency for Drugs and Technologies in Health

Centers for Medicare and Medicaid Services (CMS)

Food and Drug Administration (FDA)

Google

Institute for Clinical Systems Improvement (ICSI)

National Guideline Clearinghouse

## Appendix C. EXCLUDED ARTICLES

### Exclude at full-text review

#### *Efficacy/ effectiveness:*

Study	Reason for exclusion
1. Candido (2008) <sup>33</sup>	Prognostic study (compares the interlaminar to the transforaminal approach)
2. Lee (2009) <sup>104</sup>	Prognostic study (compares the interlaminar to the transforaminal approach)
3. Manchikanti (2010) Protocol... <sup>129</sup>	Study design only (no results)
4. Murata (2009) <sup>148</sup>	The injection type used was not clear; we could not be certain it was epidural based on a number of limitations
5. Castagnera (1994) <sup>35</sup>	Uncontrolled (epidural steroid injection with or without morphine)
6. Pasqualucci (2007) <sup>159</sup>	Uncontrolled (single injection versus continuous infusion of steroids)
7. Torstensson (2009) <sup>201</sup>	Injection was intramuscular (around the sacrospinous ligament)

#### *Safety:*

Study	Reason for exclusion
1. Trentman (2009) <sup>202</sup>	Approximately 50% of pts had spondylolysis
2. White (1980) <sup>216</sup>	The percent of pts with spondylosis, spondylolisthesis, and cancer was NR
3. Botwin (2003) <sup>23</sup>	89/157 pts had spondylosis; results presented separately for HNP pts but there were only n = 68, so exclude as N < 100
4. Cicala (1989) <sup>43</sup>	The percent of pts with spondylosis was not reported
5. Derby (2004) <sup>49</sup>	Retrospective survey of interventionalists; the data was obtained from physician memory/recall only (unreliable source) instead of patient records
6. Gilula (2007) <sup>67</sup>	Technical note
7. Scanlon (2007) <sup>177</sup>	Retrospective survey of interventionalists; the data was obtained from physician memory/recall only (unreliable source) instead of patient records
8. Wagner (2005) <sup>209</sup>	Technical note

#### *Special populations:*

Study	Reason for exclusion
1. Huston (2009) <sup>88</sup>	Review with no primary data
2. Novak (2008) <sup>155</sup>	SR evaluating timing. No articles found in the SR addressing the topic.
3. Lillius (1990) <sup>108</sup>	Factors associated with both facet joint injections and sham treatment mixed
4. Revel (1992) <sup>168</sup>	Article's purpose diagnostic, not therapeutic

*Economic:* no studies excluded at full-text level

## Appendix D. LEVEL AND STRENGTH OF EVIDENCE DETERMINATION

### Methods for critical appraisal and level of evidence assessment

The method used for assessing the quality of evidence of individual studies as well as the overall quality of evidence incorporates aspects of rating scheme developed by the Oxford Centre for Evidence-based Medicine,[Phillips] precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group [Atkins, 2004] and recommendations made by the Agency for Healthcare Research and Quality (AHRQ) [West]. Taking into account features of methodological quality and important sources of bias combines epidemiologic principles with characteristics of study design.

### Procedures for determining adherence to level of evidence (LoE) criteria

Each study was rated against pre-set criteria that resulted in an evidence rating (Level of Evidence I, II (IIa or IIb), III, or IV) and presented in a table. For therapeutic and prognostic articles, the criteria are listed in the Table below. All criteria met are marked. A “+” signifies that the criterion was present, a “–” indicates that the criterion was not present, and “+/-” indicates that the reviewers could not be determine whether the criterion was met.

After the Level of Evidence was judged, the study could be upgraded or downgraded using the following:

Upgrade: Large effect size, dose response

Downgrade: limitations in study execution, indirectness of evidence

### Definition of the different levels of evidence for articles on therapy and prognosis

Studies of Therapy			Studies of Prognosis	
Level	Study design	Criteria	Study design	Criteria
<b>I</b>	Good quality RCT	<ul style="list-style-type: none"> <li>• Random sequence generation</li> <li>• Allocation concealment</li> <li>• Intent-to-treat analysis</li> <li>• Blind or independent assessment for important outcomes</li> <li>• Co-interventions applied equally</li> <li>• F/U rate of 80%+</li> <li>• Adequate sample size</li> </ul>	Good quality cohort	<ul style="list-style-type: none"> <li>• Prospective design</li> <li>• Patients at similar point in the course of their disease or treatment</li> <li>• F/U rate of 80%+</li> <li>• Patients followed long enough for outcomes to occur</li> <li>• Controlling for extraneous prognostic factors*</li> </ul>
	Moderate (IIa) or Poor (IIb) quality RCT	<ul style="list-style-type: none"> <li>• Violation of one of the criteria for good quality RCT</li> <li>• Violation of two or more criteria for a good quality RCT</li> </ul>	Moderate quality cohort	<ul style="list-style-type: none"> <li>• Prospective design, with violation of one of the other criteria for good quality cohort study</li> <li>• Retrospective design, meeting all the rest of the criteria in level I</li> </ul>
<b>II</b>	Good quality cohort	<ul style="list-style-type: none"> <li>• Blind or independent assessment in a prospective study, or use of reliable data* in a retrospective study</li> <li>• Co-interventions applied equally</li> <li>• F/U rate of 80%+</li> <li>• Adequate sample size</li> <li>• Controlling for possible confounding†</li> </ul>	Poor quality cohort	<ul style="list-style-type: none"> <li>• Prospective design with violation of 2 or more criteria for good quality cohort, or</li> <li>• Retrospective design with violation of 1 or more criteria for good quality cohort</li> </ul>
	Moderate or poor quality cohort	<ul style="list-style-type: none"> <li>• Violation of any of the criteria for good quality cohort</li> </ul>	Case-control	<ul style="list-style-type: none"> <li>• Any case-control design</li> </ul>
<b>III</b>	Case-control	<ul style="list-style-type: none"> <li>• Any case-control design</li> </ul>	Case series	<ul style="list-style-type: none"> <li>• Any case series design</li> </ul>
	Case series	<ul style="list-style-type: none"> <li>• Any case series design</li> </ul>		
<b>IV</b>				

\*Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

### Assessment check list for HTAs, systematic reviews and meta-analyses

Methodological Principle*	
Purpose, aim, study question, and/or hypothesis stated	
Literature search described	
Unpublished sources sought	
Inclusion/exclusion criteria stated	
Characteristics of included studies provided	
Quality of included studies formally assessed and method described	
Overall quality of included studies (LoE) given primary purpose/aim	
<b>Quantitative analysis</b>	
• Studies appraised critically	
• Magnitude and direction of effect sizes evaluated	
• Consistency of effect sizes evaluated	
• Stability of effect sizes (e.g. confidence intervals) evaluated	
• Scientific quality of studies considered in conclusions	
• Methods to enhance objectivity incorporated	
<b>Quantitative analysis</b>	
• Heterogeneity evaluated	
• Heterogeneity explored, if present	
• Missing data handled appropriately	
• Effect sizes pooled appropriately	
• Sensitivity analysis conducted	
• Publication bias explored	
Potential conflict of interest stated	

### \*Description of Methodological Principle for SRs and HTAs

#### Report type:

The type and purpose of the report influence the extent to which some of the factors listed above are applicable. For instance, for some purposes, quantitative analysis and statistical pooling may not be possible, necessary or appropriate.

**Health Technology Assessments (HTAs) and similar reports** are those which systematically evaluate the effectiveness, safety, cost implications and other properties of technology use (frequently therapeutic or diagnostic technologies) in health care, generally with respect to competing alternatives. HTA methods generally include formal systematic search for and critical appraisal of medical literatures and may include meta-analytic techniques for combining data across studies. HTAs and similar reports are frequently done by governmental agencies and/or commissioned by such agencies from private vendors. The primary purpose is to advise or inform technology-related decision and policy-making in a variety of settings, including individual (e.g. patient and/or provider) and institutional (provider organizations, health plans, government agencies) on local, regional, national or international levels.

**Systematic review** is a general term used to describe focused summaries of medical literature to address specific clinical questions using explicit strategies for literature search, inclusions and exclusions of studies and documentation of processes used to find and summarize data from the medical literature. Systematic reviews may or may not include formal meta-analysis and pooling of data.

**Meta-analysis** is a term used for systematic reviews which use quantitative, statistical methods to pool data to summarize results across studies. A systematic review generally forms the basis of meta-analysis in that a formally systematic approach to finding and selecting relevant studies for summarization is done. Pooling of data across studies may enhance statistical power to detect differences between groups. The quality of the studies to be pooled and potential for bias based on methodological flaws in individual studies needs to be considered. Methods for pooling studies (or individual patient data from a number of studies) should be stated and appropriate for the types of data and studies from which they come. Heterogeneity across studies can compromise the credibility of the pooled estimate. Heterogeneity can be related to clinical, patient or study characteristics which may or may not manifest in statistical heterogeneity. Formal evaluation and exploration of statistical heterogeneity should be done using accepted methods and modeling done accordingly (e.g. use of random effects model instead of fixed model). In evidence-based medicine, meta-analyses of the highest quality studies (usually RCTs) is considered to the highest level of evidence, however, limitations of meta-analysis should also be considered.

**Pooled analyses** frequently combine outcomes from individual patients enrolled in primary studies, the patient is the unit of analysis. These analyses may not be part of a complete systematic review of the literature. As with meta-analyses, tests for homogeneity should be done and the basis of pooling should be well described.

#### **Criteria:**

1. **Purpose, aim,** study (or key) questions and/or hypothesis for the report or analysis should be stated clearly.
2. **The literature search** should be described including timing of the search, data sources searched and search strategies used.
3. **Inclusion and exclusion criteria** for included studies should be stated and relevant to the purpose and questions to be addressed in the report and consistent with accepted methods for conduct of the type of report.
4. **Characteristics of included studies** should be given with regard to study design, populations studied and technologies applied as relevant to the report's purpose and aims.
5. **Quality of included studies** should be formally assessed using a specified system for evaluation that takes into account study design, potential sources of bias, methodological limitations, statistical power and use of appropriate analyses (e.g. controlling for confounding), usually leading to an overall score, classification or grade of evidence.

6. **The Level of Evidence (LoE)** of individual studies included should be the highest possible based on the primary focus of the report. Spectrum Research's LoE criteria are described below. If all included studies are RCTs (randomized controlled trials), the LoE using Spectrum Research's approach is either I or II. For trials of surgery or other interventions where clinician and/or patients are not blinded, the LoE is often II, since there is the opportunity for bias in assessment by the clinician and/or bias in patient response. Whether this criterion is met depends on the primary outcome and whether it could have been assessed in a blinded fashion. Subanalyses of RCTs are considered LoE II/III since randomization is generally not preserved. Registry studies are primarily retrospective cohort studies and subject to bias from a variety of sources and are classified as LoE III.
7. **Qualitative analysis:** Some reports may primarily provide qualitative assessment of included studies. Systematic reviews and meta-analyses should incorporate most of these components. The extent to which the following criteria are met provides some indication of the overall quality of the assessment
  - **Critical appraisal of included studies** – The report should describe a formal method of evaluating individual quality with regard to study design, methodological issues and potential for bias, such as the LoE system described below. A “grade” or other classification of study quality should be described and applied across studies.
  - **Evaluation of estimate magnitude and direction:** The report should accurately interpret and describe these, including statistical significance and any statistical adjustments to effect size estimates.
  - **Estimate consistency:** Reports should describe the general patterns of effect size estimates across studies and how consistent they are. Reports should describe if estimates from different studies have the same general direction and magnitude across studies or not.
  - **Estimate stability:** Reports should comment on the general stability of estimates, based in consideration of things like confidence intervals, effects of missing data, study sample size, confounding and other factors which may influence estimate stability
  - Consideration of the **overall scientific quality** of the evidence for a specific question: Do the report's conclusions consider the overall strength of evidence based on the scientific quality of the studies, the consistency, direction and magnitude of the estimates used to formulate the conclusions?
8. **Quantitative analysis:** This involves the statistical combining and evaluation of data from multiple studies and applies to situations where meta analysis is done.
  - **Pooling** of data may or may not be appropriate depending on the types of studies and data available. Various methods for pooling data are possible. The report should adequately describe how pooling was done and methods used to create summary estimates should be appropriate to the data, included studies and consideration of factors such as clinical and statistical heterogeneity. Methods for study weighting and modeling of pooled estimates should be described.

- Formal meta-analysis is a structured process with specific types of methodologies for combining data, weighting studies, modeling and assessing heterogeneity across studies in order to arrive at pooled estimates of effect size.
  - Not all reports that pool data across studies are true meta-analyses from a methodological perspective.
- **Evaluation of heterogeneity.** Description of how heterogeneity was evaluated should be consistent with the type of analysis and modeling done to pool the data and specific criteria for determining heterogeneity should be described and applied. The results of heterogeneity evaluations should be stated.
  - **Exploration of heterogeneity if present:** If there is significant heterogeneity present, a description of possible sources and methods used to explore it should be described and the results reported.
  - **Missing data:** Does the report describe missing data, how it was handled and the extent to which it may influence estimate stability, which may in part be done with sensitivity analysis
  - **Sensitivity analysis:** The report should explore the stability of estimates using appropriate sensitivity analyses, including around missing data or areas of heterogeneity. Exploration of publication bias should be described as appropriate.
9. **Potential conflicts of interest:** Is the source of funding for the report stated and/or is there information on potential conflicts of interest for authors presented?

### Determination of Overall Strength of Evidence

Following the assessment of the quality of each individual study included in the report, an overall “strength of evidence for the relevant question or topic is determined. Methods for determining the overall strength of evidence for diagnostic studies are variable across the literature and are most applicable to evaluation of therapeutic studies.

SRI’s method incorporates the primary domains of quality (LoE), quantity of studies and consistency of results across studies as described by AHRQ<sup>215</sup>.

SRI establishes a strength-of-evidence baseline using the following definitions to determine whether or not the body or evidence meets the criteria for each domain:

Domain	Definition/Criterion
Quality	<ul style="list-style-type: none"> <li>At least 80% of the studies are LoE I or II</li> </ul>
Quantity	<ul style="list-style-type: none"> <li>There are at least three studies which are adequately powered to answer the study question</li> </ul>
Consistency	<ul style="list-style-type: none"> <li>Study results would lead to a similar conclusion (similar values, in the same direction) in at least 70% of the studies</li> </ul>

Based on the criteria described above, the possible scenarios that would be encountered are described below. Each scenario is ranked according to the impact that future research is likely to have on both the overall estimates of an effect and the confidence in the estimate. This ranking describes the overall “Strength of Evidence” (SoE) for the body of literature on a specific topic. The method and descriptions of overall strength are adapted for diagnostic studies from system described by the GRADE Working Group<sup>12</sup> for the development of clinical guidelines.

SoE	Description	Further Research Impact	Domain Criterion Met		
			Quality	Quantity	Consistency
1	High	Very unlikely to change confidence in effect estimate	+	+	+
2	Moderate	Likely to have an important impact on confidence in estimate and <i>may</i> change the estimate	+	-	+
			+	+	-
3	Low	Very likely to have an important impact on confidence in estimate and <i>likely</i> to change the estimate	+	-	-
			-	+	+
4	Very Low	Any effect estimate is uncertain	-	+	-
			-	-	+
			-	-	-

Limitations or special strengths can modify the quality of the evidence from the baseline as follows:

Factors that can reduce the quality of the evidence 1 or 2 levels:

- Limitations in study design or execution
- Indirectness of evidence
- Imprecision

Factors that can increase the quality of the evidence: 1 or 2 levels:

- Large magnitude of effect
- Dose response gradient

## Assessment of Economic Studies

Full formal economic analyses evaluate both costs and clinical outcomes of two or more alternative interventions. The four primary types are cost minimization analysis (CMA), cost-utility analysis (CUA), cost-effectiveness analysis (CEA), and cost-benefit analyses (CBA). Each employs different methodologies, potentially complicating critical appraisal, but some common criteria can be assessed across studies.

No standard, universally accepted method of critical appraisal of economic analyses is currently in use. A number of checklists [Canadian, BMJ, AMA] are available to facilitate critique of such studies. The Quality of Health Economic Studies (QHES) instrument developed by Ofman, et al<sup>156</sup>. QHES embodies the primary components relevant for critical appraisal of economic studies<sup>38, 156</sup>. It also incorporates a weighted scoring process and which was used as one factor to assess included economic studies. This tool has not yet undergone extensive evaluation for broader use but provides a valuable starting point for critique.

In addition to assessment of criteria in the QHES, other factors are important in critical appraisal of studies from an epidemiologic perspective to assist in evaluation of generalizability and potential sources of study bias.

Such factors include:

- Are the interventions applied to similar populations (eg, with respect to age, gender, medical conditions, etc)? To what extent are the populations for each intervention comparable and are differences considered or accounted for? To what extent are population characteristics consistent with “real world” applications of the comparators?
- Are the sample sizes adequate so as to provide a reasonable representation of individuals to whom the technology would be applied?
- What types of studies form the basis for the data used in the analyses? Data (eg, complication rates) from randomized controlled trials or well-conducted, methodologically rigorous cohort studies for data collection are generally of highest quality compared with case series or studies with historical cohorts.
- Were the interventions applied in a comparable manner (eg, similar protocols, follow-up procedures, evaluation of outcomes, etc)?
- How were the data and/or patients selected or sampled (eg, a random selection of claims for the intervention from a given year/source or all claims)? What specific inclusion/exclusion criteria or processes were used?
- Were the outcomes and consequences of the interventions being compared comparable for each? (eg, were all of the relevant consequences/complications for each intervention considered or do they primarily reflect those for one intervention?)

Assessment of the overall strength of evidence for formal economic analyses does not appear to be documented in the literature. For the purposes of this HTA, overall strength was determined by:

- Quality of the individual studies: Where the majority of quality indicators described in the QHES met and were the methods related to patient/claim selection, patient population considerations and other factors listed above consistent with a high quality design?
- Number of formal analyses (3 or more)
- Consistency of findings and conclusions from analyses across studies.

QHEs Instrument<sup>156</sup>

Study Price et al (2005) (NHS HTA)<sup>164</sup> / Arden et al (2005)<sup>7</sup>

Questions	Possible Points	Points Awarded
1. Was the study objective presented in a clear, specific, and measurable manner?	7	7
2. Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	4
3. Were variable estimates used in the analysis from the best available source (ie, randomized controlled trial - best, expert opinion - worst)?	8	8
4. If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1	1
5. Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	9
6. Was incremental analysis performed between alternatives for resources and costs?	6	6
7. Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	5
8. Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	0
9. Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	8
10. Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes included?	6	0
11. Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	7
12. Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	8
13. Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	7
14. Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	0
15. Were the conclusions/recommendations of the study justified and based on the study results?	8	8
16. Was there a statement disclosing the source of funding for the study?	3	0
<b>TOTAL POINTS</b>	<b>100</b>	<b>78</b>

QHES Instrument<sup>156</sup>

Study Karppinen et al (2001)<sup>94, 95</sup>

Questions	Possible Points	Points Awarded
1. Was the study objective presented in a clear, specific, and measurable manner?	7	0
2. Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	0
3. Were variable estimates used in the analysis from the best available source (ie, randomized controlled trial - best, expert opinion - worst)?	8	8
4. If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1	0
5. Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	0
6. Was incremental analysis performed between alternatives for resources and costs?	6	6
7. Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	5
8. Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	0
9. Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	0
10. Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes included?	6	6
11. Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	7
12. Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	8
13. Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	0
14. Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	6
15. Were the conclusions/recommendations of the study justified and based on the study results?	8	0
16. Was there a statement disclosing the source of funding for the study?	3	3
<b>TOTAL POINTS</b>	<b>100</b>	<b>49</b>

## Appendix E. LEVEL OF EVIDENCE FOR COMPARATIVE STUDIES

### Methodological quality of therapeutic studies evaluating efficacy or effectiveness following spinal injections.

Methodological principle	Manchikanti 2008 <sup>132</sup> (pt 2)	Manchikanti 2010 <sup>136</sup> (Eval. of the effect...)	Sayegh 2009 <sup>176</sup>	Manchikanti 2008 <sup>118</sup> (pt 1)
<b>Study design</b>				
Randomized controlled trial	+	+	+	+
→ Random sequence generation	+	+	-	+
→ Allocation concealment	-	-	-	-
→ Intention to treat	-	+	+	-
Cohort study				
Case series				
<b>Other Methods Implementation</b>				
Independent or blind assessment	+	+	+	+
Co-interventions applied equally	-	-	+/-	-
Complete follow-up of $\geq 80\%$	-	-	+	-
Adequate sample size	+	+	+	+
Controlling for possible confounding†	-	-	+	+
<b>Evidence class</b>	<b>I Ib</b>	<b>I Ib</b>	<b>I Ib</b>	<b>I Ib</b>

Methodological principle	Manchikanti 2010 <sup>116</sup> (Prelim. results...)	Manchikanti 2008 <sup>115</sup> (pt 4)	Manchikanti 2008 <sup>133</sup> (pt 3)	Ghahreman 2010 <sup>64</sup>
<b>Study design</b>				
Randomized controlled trial	+	+	+	+
→ Random sequence generation	+	+	+	+
→ Allocation concealment	-	-	-	-
→ Intention to treat	+	-	-	+
Cohort study				
Case series				
<b>Other Methods Implementation</b>				
Independent or blind assessment	+	+	+	+
Co-interventions applied equally	-	-	-	-
Complete follow-up of $\geq 80\%$	-	-	-	+
Adequate sample size	-	+	+	+
Controlling for possible confounding†	-	+	+	-
<b>Evidence class</b>	<b>I Ib</b>	<b>I Ib</b>	<b>I Ib</b>	<b>I Ib</b>

(continued)

Methodological principle	Tafazal 2009 <sup>197</sup>	Manchikanti 2009 <sup>117</sup> (The prelim. results...)	Manchikanti 2009 <sup>134</sup> (A comparative effect...)	Koc 2009 <sup>99</sup>
<b>Study design</b>				
Randomized controlled trial	+	+	+	+
→ Random sequence generation	+	+	+	-
→ Allocation concealment	-	-	-	-
→ Intention to treat	-	-	-	+
Cohort study				
Case series				
<b>Other Methods Implementation</b>				
Independent or blind assessment	+	+	+	-
Co-interventions applied equally	+	-	-	+
Complete follow-up of $\geq 80\%$	+	-	-	+
Adequate sample size	-	+	+	+/-
Controlling for possible confounding†	+	+	-	-
<b>Evidence class</b>	<b>IIb</b>	<b>IIb</b>	<b>IIb</b>	<b>IIb</b>

Methodological principle	Manchikanti 2010 <sup>135</sup> (Evaluation of lumbar...)	Peng 2010 <sup>161</sup>	Manchikanti 2010 <sup>125</sup> (The effectiveness of fluor...)	Manchikanti 2010 <sup>124</sup> (Cervical epidural...)
<b>Study design</b>				
Randomized controlled trial	+	+	+	+
→ Random sequence generation	+	+	+	+
→ Allocation concealment	-	-	-	-
→ Intention to treat	-	+	-	-
Cohort study				
Case series				
<b>Other Methods Implementation</b>				
Independent or blind assessment	+	+	+	+
Co-interventions applied equally	-	+	-	-
Complete follow-up of $\geq 80\%$	+	+	-	-
Adequate sample size	-	+	-	-
Controlling for possible confounding†	+	+	+	+
<b>Evidence class</b>	<b>IIb</b>	<b>IIa</b>	<b>IIb</b>	<b>IIb</b>

(continued)

Methodological principle	Stav 1993 <sup>193</sup>	Barnsley 1994 <sup>15</sup>	Manchikanti 2008 <sup>137</sup> (Cervical medial branch...)
<b>Study design</b>			
Randomized controlled trial	+	+	+
→ Random sequence generation	-	+	+
→ Allocation concealment	-	-	-
→ Intention to treat	+	+	+
Cohort study			
Case series			
<b>Other Methods Implementation</b>			
Independent or blind assessment	-	+	+
Co-interventions applied equally	+	+	-
Complete follow-up of $\geq 80\%$	+	+	+
Adequate sample size	+	-	-
Controlling for possible confounding†	+	+	+
<b>Evidence class</b>	<b>IIb</b>	<b>IIb</b>	<b>IIb</b>

\* Applies to randomized controlled trials only.

† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

Spectrum Research has specific pre-defined criteria that are used in grading the methodological quality of each study. The rationale for giving or not giving credit for specific methodological principles for each therapeutic study is stated in section 3.2.3.

(continued)

**Methodological quality of therapeutic studies comparing interlaminar with transforaminal approaches for epidural steroid injections.**

Methodological principle	Lee 2009	Candido 2008	Smith 2010	Schaufele 2006
<b>Study design</b>				
Randomized controlled trial	+	+		
→ Random sequence generation	+	+		
→ Allocation concealment	–	–		
→ Intention to treat	–	–		
Cohort study			+	+
Case series				
<b>Other Methods Implementation</b>				
Independent or blind assessment	+	–*	–	–
Co-interventions applied equally	+	+/-	–	+/-
Complete follow-up of $\geq 80\%$	+	+	–	–
Adequate sample size	+	–	–	–
Controlling for possible confounding†	+	–	+	+
<b>Evidence class</b>	<b>Ib</b>	<b>Ib</b>	<b>III</b>	<b>III</b>

\* Blind assessment of contrast media spread, but not of clinical outcomes

**Table. Methodological quality of therapeutic studies comparing different types of injectates for epidural steroid injections.**

Methodological principle	Dreyfuss 2006	Ghahreman 2010
<b>Study design</b>		
Randomized controlled trial	+	+
→ Random sequence generation	–	+
→ Allocation concealment	–	–
→ Intention to treat	+	+
Cohort study		
Case series		
<b>Other Methods Implementation</b>		
Independent or blind assessment	–	–
Co-interventions applied equally	+/-	–
Complete follow-up of $\geq 80\%$	+	+
Adequate sample size	+	–
Controlling for possible confounding†	–	–
<b>Evidence class</b>	<b>Ib</b>	<b>Ib</b>

\*Blind assessment of contrast media spread, but not of clinical outcomes

**Methodological quality of prognostic studies assessing factors associated with outcome epidural steroid injections.**

Methodological principle	Rivest 1998	Lee 2010	Kwon 2007	Lee 2006	Ferrante 1993
Study design					
Prospective cohort study	+				
Retrospective cohort study		+	+	+	+
Case-control study					
Case-series					
Patients at similar point in the course of their disease or treatment	+	+/-	+	+	+
Patients followed long enough for outcomes to occur	+	+	+	+	+
Complete follow-up of $\geq 80\%$	-	-	-	-	+/- <sup>†</sup>
Controlling for extraneous prognostic factors*	-	-	+	+	+
<b>Evidence class</b>	<b>III</b>	<b>III</b>	<b>III</b>	<b>III</b>	<b>III</b>

\* Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

<sup>†</sup> 80% at 6 months follow-up, 53% at 12 month follow-up

### Methodological quality of systematic reviews evaluating efficacy of spinal injections

Methodological principle	Chou (2009) APS evidence report
Purpose, aim, study question and/or hypothesis stated	✓
Literature search described	✓
Unpublished sources sought	
Inclusion/exclusion criteria stated	✓
Characteristics of included studies provided	
Quality of included studies formally assessed and method described	✓ (I/II)
<b>Quantitative analysis</b>	
• Studies appraised critically	✓
• Magnitude and direction of effect sizes evaluated	✓
• Consistency of effect sizes evaluated	✓
• Stability of effect sizes (e.g. confidence intervals evaluated)	
• Scientific quality of studies considered in conclusions	✓
• Methods to enhance objectivity incorporated	✓
<b>Qualitative analysis</b>	
• Heterogeneity evaluated	✓
• Heterogeneity explored, if present	n/a
• Missing data handled appropriately	
• Effect sizes pooled appropriately	✓
• Sensitivity analysis conducted	
• Publication bias explored	
Potential conflict of interest stated	✓

n/a: not applicable

Spectrum Research has specific pre-defined criteria that are used in grading the methodological quality of each study. The rationale for not giving credit for specific methodological principles for each systematic review is stated in section 3.2.2.

## Appendix F. Summary of Manchikanti et al (2010) critical appraisal of the Chou et al (2009) APS evidence report

This review essentially repeated what Dr. Chou had done but reevaluated the evidence using similar but somewhat different methodologies, which are compared with Chou's methodologies below (differences highlighted in bold):

	Chou et al. (2009): APS SR <sup>39, 40</sup>	Manchikanti et al (2010) <sup>128</sup> : critical review
Literature search	1966 - July, 2008	1966 - 2009
Selection criteria	Systematic reviews and RCTs	(same)
Short-term versus long-term	Short-term: < 3 months Long-term: ≥ 3 months	<b>Short-term: ≤ 6 months</b> <b>Long-term: &gt; 6 months</b>
Outcome measures	At least one of the following: <ul style="list-style-type: none"> <li>• Back-specific function</li> <li>• Generic health status</li> <li>• Pain</li> <li>• Work disability</li> <li>• Patient satisfaction</li> </ul>	<b>Primary outcome measure:</b> <ul style="list-style-type: none"> <li>• <b>Pain relief</b></li> </ul> <b>Secondary outcome measures:</b> <ul style="list-style-type: none"> <li>• <b>Functional improvement</b></li> <li>• <b>Psychological improvement</b></li> <li>• <b>Improvement in work status</b></li> <li>• <b>complications</b></li> </ul>
Methodologic assessment of systematic reviews	Oxman and Guyatt, adapted by Furlan	same
Methodologic assessment of systematic reviews	Cochrane Back Review Group	same
Analysis of strength of evidence	USPSTF (United States Preventative Services Task Force) method	same
Data synthesis & outcomes	<u>Positive efficacy</u> : the intervention is beneficial <u>Negative efficacy</u> : the intervention is harmful or not beneficial <u>Uncertain efficacy</u> : imprecise estimates, unclear evidence, or inconsistent results ("inconsistency" = > 25% (or ≥2) of higher-quality studies reaching discordant conclusions <u>or</u> unexplained heterogeneity)	<b>Positive: the intervention is effective in terms of pain relief compared with either a placebo or active control (<math>P &lt; .05</math>)</b> <b>Negative: no difference between groups <u>or</u> no improvement from baseline</b>

The relevant interventions examined in this review<sup>128</sup> included epidural steroid injections, facet joint injections and therapeutic medial branch blocks (intradiscal steroid injections and therapeutic sacroiliac joint interventions were not evaluated); the author's main points are summarized below:

- **Epidural steroid injections:**
  - Manchikanti believes each approach (caudal, interlaminar, and transforaminal epidural injections) must be considered separately; Chou combined these into one category and reached inaccurate conclusions that these treatments were only effective in the short-term

- Manchikanti wrote that results must be considered separately for different pathologies (ie., disc herniation and/or radiculitis, discogenic pain without disc herniation, spinal stenosis, and lumbar post surgery syndrome)
- ***Caudal epidural steroid injections:***
  - Disc herniation and radiculitis: Manchikanti concluded that “there is fair evidence for the therapeutic effectiveness of caudal epidural steroid injections, in patients with disc herniation or radiculitis with or without steroids, for short-term and long-term relief,” and that addition of new studies increases the strength of the evidence from fair to good. Manchikanti evaluated seven of the eight trials included in the APS review (except for Zahaar, since “the methodologic criteria was low and it was not placebo controlled, a feature misunderstood by APS guidelines”). Two additional studies published after July 2008 were also included.
  - Post-surgery syndrome: there were no apparent differences in conclusions between the reviews.
  - Spinal stenosis: one recent randomized trial (published after Chou’s report) may change the evidence.
  - Discogenic pain: there were no apparent differences in conclusions between the reviews.
- ***Interlaminar epidural steroid injections:*** There were no apparent differences in conclusions between the reviews, though Manchikanti believes that these types of injections should have been evaluated separately from caudal epidural steroid injections.
- ***Transforaminal epidural injections:*** Manchikanti concluded that short-term results were positive in four of the five studies and that long-term results were positive in one of two studies of the studies; based on the evidence, Manchikanti determined that “the evidence appears to be fair.” Manchikanti included one study not included in the APS assessment “as it was rated as high quality by Chou”.
- ***Facet joint injection and therapeutic medial branch blocks:***
  - For intraarticular injections, Manchikanti noted that all five RCTs included in the APS report did not meet inclusion criteria laid out by another systematic review (Datta) as none of them utilized controlled diagnostic blocks.
  - Manchikanti was in agreement with the APS report regarding the efficacy of intraarticular injections.
  - Of the four studies used to evaluate the efficacy of medial branch blocks, Manchikanti noted that two studies reported only short-term outcomes and did not utilize diagnostic blocks, and that one of these two studies was excluded in other systematic reviews.

- After a reassessment of the evidence, Manchikanti concluded that there was fair evidence supporting the use of therapeutic lumbar facet joint nerve blocks.

## **Appendix G. Chou's response to the Manchikanti et al (2010) critical appraisal of the Chou et al (2009) APS evidence report**

### **Response to critiques of the American Pain Society guideline on interventional therapies by the American Society of International Pain Physicians.**

In 2009, a guideline sponsored by the American Pain Society (APS) on use of interventional procedures for low back pain was published in *Spine*<sup>41</sup>, along with a summary<sup>39</sup> of the evidence review on which the guideline was based. The full evidence review was subsequently posted on the APS website<sup>39</sup>. The evidence review and guideline found insufficient evidence to make recommendations for invasive diagnostic tests and a number of interventional procedures.

The American Society of Interventional Pain Physicians (ASIPP), led by Manchikanti et al, recently published a lengthy critique<sup>128</sup> of the APS guideline. The critique sought to challenge the methods used to develop the APS guideline, point out alleged errors in the evidence review, and raise concerns about the integrity of the APS guideline development process. However, the ASIPP document contains many inaccurate statements and methodological errors which render the criticisms invalid, and I stand behind the work conducted to develop the APS guideline.

#### **Inaccurate statements**

The ASIPP critique includes a number of erroneous and misleading statements<sup>128</sup>.

- The ASIPP critique states that Dr. Chou, the lead author on the APS guidelines, is employed by the Agency for Healthcare Research and Quality (AHRQ) and didn't provide this information. In fact, as described in the guideline and related publications, Dr. Chou is employed by the Oregon Health & Science University. He is not a federal employee, although he, like many individuals in the academic and private sectors, has received research funding from government organizations such as AHRQ. Describing him as a federal employee would be like stating that any individual who ever received funding from the National Institutes of Health is a federal employee.
- The ASIPP critique also suggests that Dr. Chou and other members of the guideline development group are methodologists and not clinicians, when in fact most are both. Regardless, the suggestion in the ASIPP critique that methodologists are less concerned than clinicians with accurate determinations of the evidence or helping people with pain is baseless and offensive.
- The assertion in the ASIPP critique that other undisclosed professional societies may have co-sponsored the APS guideline was due in part to an error in the heading of the APS evidence review<sup>42</sup>. As stated in the guideline and accompanying articles, APS was in fact the sole sponsor<sup>39-41</sup>. Although the American College of Physicians co-sponsored an earlier guideline<sup>42</sup> on initial evaluation and management of low back pain, they were

not co-sponsors of the interventional therapies guideline. The American Academy of Pain Medicine also was not involved.

- The statement in the ASIPP critique that conflict of interest policies and external peer review were not described is erroneous, as this information is provided in the guideline<sup>41</sup>.
- The assertion that certain members of the APS guideline panel withdrew their support is inaccurate. ASIPP instructed one expert whom they had nominated to work with APS on the guideline to not be listed as an author (a violation of editorial independence). He did not withdraw from the panel and agreed to be listed as a full participant. A full list of panel members and potential conflicts of interest was submitted for inclusion as electronic supplements to the guideline, but inadvertently left out of the journal publication (though available to anyone who requested it); this list is available below this response.
- The assertion in the ASIPP critique that the APS review drew conclusions regarding the efficacy of interventional procedures based on previously published systematic reviews is incorrect. Rather, as described in the methods<sup>39-41</sup>, the source of evidence for determining efficacy was randomized, placebo- or sham-controlled trials. Previously published systematic reviews were described to provide context and to help identify and explore potential areas of discordance between our review and others<sup>217</sup>.
- There are also errors when the ASIPP critique disputes the findings from the APS review regarding specific studies. For example, for a trial of radiofrequency denervation, the ASIPP critique<sup>128</sup> contests the statement in the APS review that final pain scores in the active and sham denervation groups were identical. The results speak for themselves: generalized pain 4.1 vs. 4.0, back pain 3.9 vs. 3.7, and leg pain 2.7 vs. 2.6.

### Application of APS methods

A large part of the ASIPP critique consists of re-applying of APS methods to studies included in the APS evidence review<sup>127, 128</sup>. Discrepancies between the ASIPP and APS reviews (for example, difference in quality ratings) are described as “errors” of the APS review. However, the ASIPP critique incorrectly applied APS methods, making this characterization invalid.

- As an example, we examined differences in quality criteria in the first randomized trial (by Mathews et al<sup>138</sup>) discussed in the ASIPP critique where there was a substantial disagreement between quality ratings from APS (quality score 4 out of 11)<sup>39</sup> and ASIPP (8 out of 11)<sup>128</sup>. There are substantial discrepancies between how the quality criteria were pre-defined in the APS review<sup>40</sup> and how they were applied in the ASIPP critique. The ASIPP critique rated the randomization criterion as “yes” even though the randomization method is not described (the criterion requires description of an appropriate method, such as computer generated randomized numbers or a random numbers table)<sup>128</sup>. The drop-out criterion was rated as “yes” even though 21%

randomized to epidural injections and 41% randomized to control dropped out (the criterion requires less than 15% drop-outs overall and for drop-outs to be roughly equal). The timing of outcome assessment criterion was rated “yes” even though the trial states that “assessments were made at least four times in the first 2 weeks” without a more precise description, and no results were reported for the first 2 weeks. Finally, the intention-to-treat criterion was rated as “yes” even though 9% (5/57) of the persons randomized to epidural steroid injections or control were not included in the analysis (the criterion requires no more than 5% of randomized patients to have been excluded). Similar errors were found when reviewing how ASIPP rated the quality of other studies.

- The ASIPP critique also failed to adhere to the pre-defined inclusion and exclusion criteria described in the APS review<sup>40</sup>. For example, in evaluating caudal epidural interventions, the ASIPP critique questions the inclusion of a trial with 24 weeks of follow up because it was too short<sup>2</sup>. However, follow-up duration was not used in the APS review to determine study eligibility. Moreover, the ASIPP critique does not consistently exclude shorter duration trials, suggesting arbitrary application of this criterion. The ASIPP critique also describes the exclusion of a foreign-language article<sup>82</sup> and active-controlled trials<sup>142, 167</sup> as “errors”, despite specific exclusions for them.
- The ASIPP critique also incorrectly states that APS should have excluded a trial by Manchikanti et al since it only addressed adhesiolysis<sup>131</sup>. In fact, this trial had three arms, one of which evaluated “catheterization without adhesiolysis, followed by injection of local anesthetic, normal saline, and steroid”—i.e., an epidural steroid injection.
- The ASIPP critique incorrectly used the Oxman and Guyatt instrument<sup>157</sup> to rate the quality of systematic review by simply adding up the number of criteria met. As described in the original article<sup>157</sup> and subsequent adaptations<sup>60</sup>, the summary score is based on an assessment of the type and severity of methodological flaws. For example, if a systematic review combined studies inappropriately, the scoring instructions are that it is likely to have major flaws (i.e., a score of 3 or less on a 1 to 7 scale).
- The failure to adhere to pre-specified methods for selecting studies and properly applying quality rating criteria are serious methodological flaws when conducting systematic reviews that invalidate subsequent steps of the review process<sup>157</sup>. Critiques of systematic reviews (such as the ones from ASIPP) with such fundamental errors have to be considered similarly unreliable.

### ASIPP Methods

Even if the ASIPP critique had adhered to the pre-specified methods for selecting and rating studies, it still wouldn’t meet standards for synthesizing evidence as described by groups such as the U.S. Preventive Services Task Force<sup>78</sup>, the Cochrane Collaboration,<sup>83</sup> the Grading of

Recommendations Assessment, Development, and Evaluation (GRADE) Working Group<sup>74</sup>, and others.

- The ASIPP method for grading evidence is almost solely based on study design hierarchy<sup>128</sup>. Using study design alone to grade evidence is an outdated method. Also critical are the quality of studies, the number and size of studies, consistency between studies, and directness of evidence. One of the reasons that the ASIPP critiques came to different conclusions compared to the APS review is that the ASIPP methods largely ignore issues related to inconsistency and sparse data. Yet being able to duplicate research results from one setting to another is a core principle of the scientific process, and small studies provide imprecise estimates as well as results that are often better than observed in larger studies.
- ASIPP methods for analyzing active-controlled trials are also flawed. Rather than using them to compare one treatment to another, as they are designed to do<sup>198</sup>, they interpret improvements over time in patients who received the treatment as evidence of efficacy versus no treatment. For example, a trial by Manchikanti et al that compared a caudal epidural injections with steroid and local anesthetic versus a local anesthetic alone was described in the ASIPP critique as “positive” since both groups experienced improvement<sup>132</sup>. This approach eliminates the benefits of randomization, essentially reducing the trials to uncontrolled, before-after time series—one of the weakest types of evidence. Nonetheless, the ASIPP critique suggests that conclusions drawn in this way are equivalent to results showing that an intervention is superior to a placebo or sham treatment in a randomized trial.
- The ASIPP critique<sup>128</sup> advocates a weighted scoring system for rating the quality of randomized trials based on the Cochrane Back Review Group criteria, describing it as superior to the unweighted system used by the APS review. In fact, there is no evidence supporting use of a weighted system, a recent study supports the unweighted scoring system<sup>206</sup>, and the Cochrane Back Review Group does not recommend using a weighted system<sup>61</sup>.
- The ASIPP critique incorrectly refers to a report by West et al<sup>215</sup> as providing AHRQ criteria for evaluating the quality of various studies. The West et al study was a systematic review commissioned by AHRQ to assess the usefulness of existing quality rating systems. It was never designed to provide quality rating instruments and have never been endorsed by AHRQ as such.
- The ASIPP critiques mix issues related to external validity with quality (internal validity)<sup>173</sup>. For example, in the section on caudal epidural injections<sup>128</sup>, they describe studies with short duration of follow-up, lack of placebo-control, or use of high volume

injections as poor-quality even though none of these issues are associated with bias per se.

**Members of the American Pain Society Low Back Pain Interventional and Surgical Therapies Panel, specialty area and affiliation**

**Paul M. Arnstein, RN, PhD, APRN-BC** - Nursing, Boston College

**Steven J Atlas, MD, MPH** - Internal Medicine, Harvard Medical School

**Jamie L. Baisden, MD, FACS** - Neurosurgery, Medical College of Wisconsin

**Claire Bombardier, MD, FRCPC** - Rheumatology, University of Toronto

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**John Anthony Carrino, MD, MPH** - Radiology, Johns Hopkins University Medical Center

**Daniel Cherkin, PhD** - Complementary and Alternative Medicine Research, Center for Health Studies - Group Health Cooperative

**Penney Cowan** - Patient/consumer Representative, American Chronic Pain Association

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**Appendix H. Correspondence with Dr. Manchikanti regarding study methodology**

October 8, 2010

Robin Hashimoto, MD

[robin@specri.com](mailto:robin@specri.com)

RE: Questions re: RCTs for WA HTA (spinal injections)

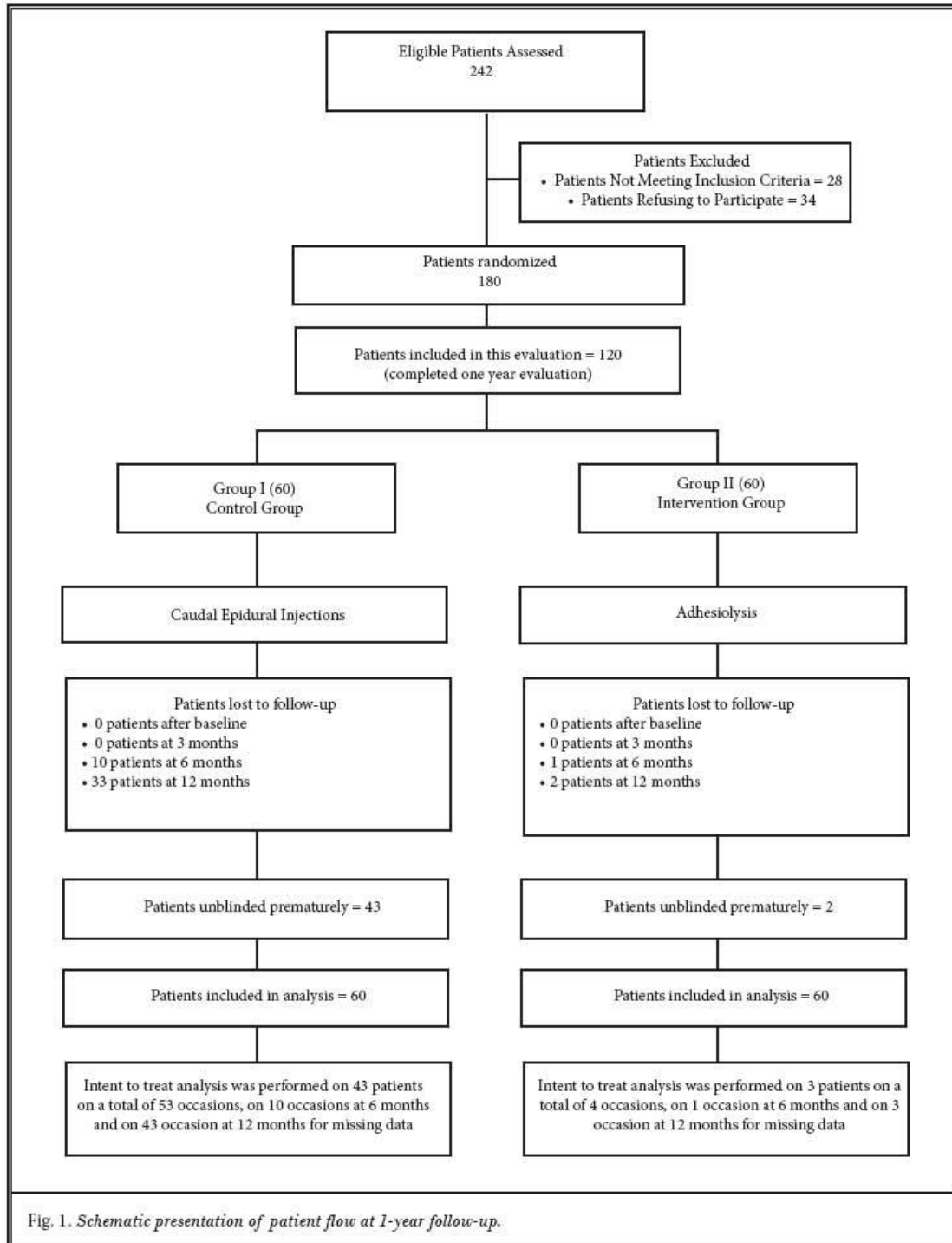
Dear Dr. Hashimoto:

Thank you for your letter. I'm impressed with your detailed analysis. However, please do not discount the article just based on withdrawals in the control group. That is a natural phenomenon in chronic pain management. No one wants to wait 2 years if their treatment is not working. Of course there are always exceptions and some people who may still want to wait. The following are the responses to your questions:

**QUESTION 1:** At the time of the study, you randomized 180 patients, yet only included 120. It is stated that <sup>3</sup>all the patients completing one-year follow-up were selected by the statisticians<sup>2</sup> What criteria did the statistician use to select these? Can you tell me about the 60 that were not included? Why were they excluded? If they did not complete one year evaluation, can you tell me why? Also, can you tell me how many of the 60 patients not included were assigned to each treatment group?

**RESPONSE:** Randomization was performed by computed generated random allocations sequence by simple randomization. As you see from Figure 1, there were 180 patients randomized by that time. Three and a half years after the study, we looked at the number of patients who had completed one year follow-up based on their enrollment date without group assignment. There were 126 patients who had completed the evaluation. Following this, it was decided to choose 60 patients in each group who had completed the one year follow-up. Thus, the statistician took the first 60 patients completing the one year follow-up in both groups.

The answer to the second part of your question is that there were 28 patients in Group 1 and 32 patients in Group 2 with a total of 60 patients assigned but who had not yet completed one year follow-up at that time.



**QUESTION 2:** How is it that there were the same number of patients in each treatment group (n=60) given that your random allocation occurred by simple randomization? Can you clarify the allocation process for me?

**RESPONSE:** As explained above, it was simple randomization; they were not equal, but we have taken 60 patients in each group to leave the numbers equal, but their differences were not that significant.

**QUESTION 3:** In Figure 1, looking at the boxes "patients lost to follow-up": are these numbers cumulative? ie., in Group I, were a total of 43 patients lost to follow-up (10 patients lost to follow-up at 6 months and then an additional 33 patients lost to follow-up at 12 months)? Or were a total of 33 patients lost to follow-up at 12 months?

**RESPONSE:** You are accurate in the analysis of Figure 1, but please do not misconstrue these withdrawals and unblindings to blame the procedure on methodologic criteria.

**QUESTION 4:** In Figure 1, were the number of patients who were unblinded prematurely accounted for in the box with the number of patients who were lost to follow-up? If so, is it accurate to assume that patients who were unblinded were also considered to be lost to follow-up?

**RESPONSE:** You are accurate for this part also. This may not be true in all cases, but it happened to be true for Group 1. For Group 2, there were 3 patients without follow up, but only 2 patients were unblinded prematurely.

**QUESTION 5:** Would we be accurate in considering the number of patients on whom <sup>3</sup>intent to treat analysis<sup>2</sup> was performed (bottom two boxes in Figure 1) as representative of all patients without complete data sets (ie., lost to follow-up)? So, for Group I, we would consider that a total of 43 patients were lost to follow-up: 0 patients at 3 months, 10 patients at 6 months, and 43 patients at 12 months- is this correct?

**RESPONSE:** This is also accurate. Once again, let us not be misled by these numbers.

**QUESTION 6:** How is your statistician defining <sup>3</sup>intent to treat<sup>2</sup> analysis?

**RESPONSE:**

The intent-to-treat analysis was performed utilizing last visit follow-up data for those patients who had dropped out of the study. Prior to choosing this methodology, we also did a sensitivity analysis of the intent-to-treat analysis data and there was no significant difference with any methodology, which included last visit values, best case values, worst case values, and the average values. Since there were no significant differences, we chose last visit values. Please see Table 2 of the attached article.

**QUESTION 7:** With respect to which patients were analyzed at different times, is the following correct (for Group I):

3-month data (n = 60): consists of 3-month data for 60 patients;

6-month data (n = 60): consists of 6-month data for 50 patients and

3-month data for the 10 patients lost to follow-up; 12-month data (n = 60): consists of 12-month data for 17 patients, 3-month data for the 10 patients lost to follow-up by 6 months and 6-month data for the 33 patients lost to follow-up by 12 months

that is, the last observation was carried forward for those patients who were lost to follow-up?

**RESPONSE:** You are accurate in your assessment. The last observation was carried forward for those patients who were lost to follow up.

If you have any further questions, please feel free to contact me.

Laxmaiah Manchikanti, MD

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<http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=search&db=pubmed&term=manchikanti>

“Man spends his life in reasoning on the past, in complaining of the present, in fearing future.”

*Antoine Rivarol*

“There is no limit to what a man can do or where he can go if he doesn’t mind who gets the credit.” *Ronald Reagan*

## Appendix I. Conflict of interest for Dr. Manchikanti (ASIPP and SIPMS)

Dr. Manchikanti is the chief executive officer, founder, and chairman of the board of ASIPP (American Society of Interventional Pain Physicians; <http://www.asipp.org/>)<sup>11</sup> and the chief executive officer and chairman of the board of SIPMS (the Society of Interventional Pain Management Surgery Centers; <http://www.sipms.org/>)<sup>181</sup>.

ASIPP is a non-profit organization which publishes the journal (Pain Physician)<sup>8</sup> in which all of these studies were published; SIPMS is an “advocacy group for physician owners of ambulatory surgery centers”. Two of the self-stated goals of ASIPP and SIPMS are to “preserve coverage for interventional pain management,” and to “communicate with legislators, patients, public, CMS, & third party payors”<sup>11, 180</sup>. SIPMS also strives to “ensure patient access to [pain management] interventions”<sup>180</sup>. Other goals of ASIPP and SIPMS are to<sup>11, 180</sup>:

- “promot[e] the development and practice of safe, high quality, cost-effective interventional pain management techniques”
- “advance patient safety, cost-effectiveness, and accountability,”
- “provide state of the art interventional pain management services,”
- “uphold high principles, policies, and practices,”
- “pursue excellence in education in interventional pain management,”
- “improve compliance,”
- “eliminate fraud and abuse,” and
- “provide the best possible interventional pain management.”

In addition, ASIPP is supported by a number of corporations (St. Jude Medical and Medtronic (\$100,000-\$120,000 per year), Boston Scientific and Pain Medicine News (\$25,000-\$30,000 per year), and Clint Pharmaceuticals Incorporated (among others) (\$10,000-\$12,000 per year)<sup>9, 10</sup> although it appears that Dr. Manchikanti did not receive direct support from these corporations for this work.

As a peer reviewer for this HTA, Dr. Manchikanti submitted a statement of financial interests for this HTA. Dr. Manchikanti has no financial interests in ASIPP or SIPMS, as they are non-profit organizations. Dr. Manchikanti provided the following list of additional organizations in which he, his spouse, or dependent children have financial interest:

- PMCP, PSC: provides medical services (80% interest)
- Pain Care Surgery: provides surgical services (90% interest)
- Pain Management Resources, Inc.: manages medical corporation and owns 50% in Ambulatory Surgery Center, LLC (Paducah, KY) (which provides multidisciplinary surgical services)
- KSA enterprises: real estate
- Manchikanti restaurant management

## Appendix J. Inclusion and exclusion criteria from RCTs: lumbar injections

Author (Year)	Injection Approach	Inclusion Criteria	Exclusion Criteria
<b>Manchikanti (2008, part 2)</b> <sup>132</sup>	lumbar caudal epidural	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• disc herniation or radiculitis</li> <li>• chronic (<math>\geq 6</math> months) function-limiting low back and lower extremity pain</li> </ul>	<ul style="list-style-type: none"> <li>• previous lumbar surgery</li> <li>• radiculitis secondary to spinal stenosis without disc herniation</li> <li>• uncontrollable/unstable opioid use</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid.</li> </ul>
<b>Manchikanti (2010)</b> <sup>136</sup> Evaluation of the Effectiveness	lumbar interlaminar epidural	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• disc herniation or radiculitis</li> <li>• chronic (<math>\geq 6</math> months) function-limiting low back and lower extremity pain</li> </ul>	<ul style="list-style-type: none"> <li>• previous lumbar surgery</li> <li>• radiculitis secondary to spinal stenosis without disc herniation</li> <li>• uncontrollable/unstable opioid use</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid.</li> </ul>
<b>Manchikanti (2008, part 1)</b> <sup>118</sup>	lumbar caudal epidural	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• negative diagnosis of lumbar facet joint pain (used controlled facet joint nerve blocks)</li> <li>• chronic (<math>\geq 6</math> months) function-limiting low back and lower extremity pain</li> <li>• no evidence of disc herniation</li> <li>• failed to improve substantially with conservative management, including PT, chiropractic manipulation, exercises, drug therapy, and bedrest</li> </ul>	<ul style="list-style-type: none"> <li>• positive response to controlled comparative local anesthetic blocks</li> <li>• previous lumbar surgery</li> <li>• uncontrollable/unstable opioid use</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid</li> </ul>

<b>Manchikanti (2010)</b> <sup>116</sup> Preliminary Results of a Randomized	lumbar interlaminar epidural	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• negative diagnosis of lumbar facet joint pain (used controlled facet joint nerve blocks)</li> <li>• chronic (<math>\geq 6</math> months) function-limiting low back pain</li> <li>• no evidence of disc herniation</li> <li>• failed to improve substantially with conservative management, including PT, chiropractic manipulation, exercises, drug therapy, and bedrest</li> </ul>	<ul style="list-style-type: none"> <li>• positive response to controlled comparative local anesthetic blocks</li> <li>• previous lumbar surgery</li> <li>• uncontrollable/unstable opioid use</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid</li> </ul>
<b>Manchikanti (2008, pt 4)</b> <sup>115</sup>	lumbar caudal epidural	<ul style="list-style-type: none"> <li>• <math>\geq 50</math> yrs</li> <li>• evidence of spinal stenosis with radicular pain</li> <li>• chronic (<math>\geq 6</math> months) function-limiting low back and lower extremity pain</li> <li>• central stenosis either congenital or acquired</li> <li>• failed to improve substantially with conservative management, including PT, chiropractic manipulation, exercises, drug therapy, and bedrest</li> </ul>	<ul style="list-style-type: none"> <li>• previous lumbar surgery</li> <li>• spinal stenosis without radicular pain</li> <li>• neuroforaminal stenosis</li> <li>• post laminectomy and post fusion</li> <li>• uncontrollable/unstable opioid use</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid</li> </ul>
<b>Sayegh (2009)</b> <sup>176</sup>	lumbar caudal epidural	<ul style="list-style-type: none"> <li>• persistent low back pain (<math>\geq 1</math> month) with or without unilateral or bilateral sciatica</li> <li>• failed to respond well to conservative pain control measures</li> <li>• disc degeneration or herniation confirmed by MRI scans</li> </ul>	<ul style="list-style-type: none"> <li>• cauda equina or spinal stenosis</li> <li>• symptoms lasting <math>&lt; 1</math> month</li> <li>• psychosomatic diseases or any other pathology</li> </ul>
<b>Manchikanti (2008, pt 3)</b> <sup>133</sup>	lumbar caudal epidural	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• lumbar surgery prior to 6 months or earlier</li> <li>• no evidence of lumbar facet joint pain</li> <li>• chronic (<math>\geq 6</math> months post-surgery) function-limiting low back pain with or without lower extremity pain</li> <li>• failed to improve substantially with conservative management, including PT, chiropractic manipulation, exercises, drug therapy, and bedrest</li> </ul>	<ul style="list-style-type: none"> <li>• positive response to controlled comparative local anesthetic blocks</li> <li>• uncontrollable/unstable opioid use</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid</li> </ul>

<b>Manchikanti (2009)<sup>117</sup></b> Preliminary Results of a Comparative	lumbar percutaneous epidural adhesiolysis	<ul style="list-style-type: none"> <li>• <math>\geq 50</math> yrs</li> <li>• evidence of lumbar spinal stenosis with radicular pain</li> <li>• chronic (<math>\geq 6</math> months) function-limiting low back and lower extremity pain</li> <li>• failed fluoroscopically directed epidural injections</li> <li>• failed to improve substantially with conservative management, including PT, chiropractic manipulation, exercises, drug therapy, and bedrest</li> </ul>	<ul style="list-style-type: none"> <li>• previous lumbar surgery</li> <li>• central spinal stenosis without radicular pain</li> <li>• uncontrollable/unstable opioid use</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid</li> </ul>
<b>Manchikanti (2009)<sup>134A</sup></b> Comparative Effectiveness Evaluation	lumbar percutaneous epidural adhesiolysis	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• lumbar surgery prior to 6 months or earlier</li> <li>• no evidence of lumbar facet joint pain</li> <li>• chronic (<math>\geq 6</math> months post-surgery) function-limiting low back pain with or without lower extremity pain</li> <li>• failed fluoroscopically directed epidural injections</li> <li>• failed to improve substantially with conservative management, including PT, chiropractic manipulation, exercises, drug therapy, and bedrest</li> </ul>	<ul style="list-style-type: none"> <li>• facet joints, uncontrollable as sole pain generators</li> <li>• uncontrollable/unstable opioid use (400 mg morphine equivalents/day)</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid</li> </ul>
<b>Koc<sup>99</sup> (2009)</b>	lumbar interlaminar epidural	<ul style="list-style-type: none"> <li>• evidence of lumbar spinal stenosis diagnosed by medical history, physical and neurologic exam, and MRI</li> </ul>	<ul style="list-style-type: none"> <li>• coronary artery or peripheral artery disease</li> <li>• spinal surgery</li> <li>• recent vertebral fracture</li> <li>• progression neurologic deficit</li> <li>• cauda equine syndrome</li> </ul>
<b>Ghahreman (2010)<sup>64</sup></b>	lumbar transforaminal epidural	<ul style="list-style-type: none"> <li>• adult capable of providing consent and complying with the outcome instruments used</li> <li>• pain radiating into lower limb of a lancinating, burning, stabbing, or electric quality (neurological signs of radiculopathy were not required)</li> <li>• limitation of straight-leg-raise to less than <math>30^\circ</math> (or <math>&lt; 45^\circ</math> only if there was a clear history of lancinating pain and imaging demonstrating disc herniation)</li> <li>• demonstration of disc herniation by CT or MRI at segmental level consistent with clinical features</li> <li>• eligible for surgery</li> </ul>	<ul style="list-style-type: none"> <li>• foraminal stenosis (lateral recess stenosis was acceptable only if the patient had a disc herniation affecting the target nerve)</li> <li>• sever motor deficit</li> <li>• history of substance abuse</li> <li>• inability to comply with instruments for outcome assessment</li> <li>• previous surgery at affected level</li> <li>• conditions that contraindicated spinal injection (ie., pregnancy, recent infection, or spinal deformity)</li> <li>• absence of lancinating pain in lower limb</li> </ul>

<b>Tafazal (2009)</b> <sup>197</sup>	lumbar transforaminal epidural	<ul style="list-style-type: none"> <li>• unilateral leg pain</li> <li>• MRI diagnosis of lumbar disc herniation or foraminal stenosis</li> <li>• <math>\geq 6</math> weeks of failed conservative treatment</li> <li>• leg pain intensity at least comparable to back pain intensity</li> </ul>	<ul style="list-style-type: none"> <li>• acute back trauma</li> <li>• cauda equina syndrome</li> <li>• active local skin infection</li> <li>• previous back operation</li> <li>• peri-radicular infiltration during previous 12 months</li> <li>• epidural injection in last 3 months</li> <li>• pregnancy</li> <li>• allergy to treatment agents</li> <li>• anticoagulation treatment</li> <li>• inability to complete spine assessment questionnaire</li> </ul>
<b>Manchikanti (2010)</b> <sup>135</sup> Evaluation of Lumbar Facet	lumbar facet block	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• positive diagnosis of lumbar facet joint pain (used controlled facet joint nerve blocks)</li> <li>• chronic (<math>\geq 6</math> months) function-limiting low back and lower extremity pain</li> </ul>	<ul style="list-style-type: none"> <li>• radicular pain</li> <li>• previous lumbar surgery within previous 3 months</li> <li>• heavy opioid use (morphine equivalent of 300 mg)</li> <li>• uncontrolled psychiatric disorder/depression or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• patients unable to assume the prone position</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics, steroid, or Sarapin</li> </ul>
<b>Peng</b> <sup>161</sup> (2010)	lumbar intradiscal	<ul style="list-style-type: none"> <li>• chronic low back pain without radiculopathy</li> <li>• evidence of lumbar disc degeneration on MRI scan</li> <li>• failed to have more than 6 months pain free with conservative management, including PT and drug therapy</li> <li>• no previous lumbar surgery</li> <li>• exhibited normal or slight decrease in height of disc space on lateral X-ray</li> </ul>	<ul style="list-style-type: none"> <li>• lumbar disc herniation*</li> <li>• spinal instability*</li> <li>• lumbar canal stenosis*</li> <li>• spondylolysis*</li> <li>• spondylolisthesis (isthmic or degenerative) *</li> <li>• disc degeneration with endplate Modic changes*</li> <li>• neurologic disease*</li> <li>• inflammatory arthritis*</li> <li>• tumor*</li> <li>• infection*</li> <li>• psychological problems (depression or taking antidepressants/anxiolytic drugs for treatment of depression)</li> </ul>

NSAID: Nonsteroidal Anti-Inflammatory Drug

MRI: magnetic resonance imaging

PT: physical therapy

\*Based on history, clinical examinations, and imaging [Peng, 2010].

## Appendix K. Inclusion and exclusion criteria from RCTs: cervical injections

Author (Year)	Injection Approach	Inclusion Criteria	Exclusion Criteria
<b>Manchikanti (2010)</b> <sup>124</sup> Cervical Epidural Injections	cervical interlaminar epidural	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• negative diagnosis of cervical facet joint pain (used controlled facet joint nerve blocks)</li> <li>• chronic (<math>\geq 6</math> months) function-limiting neck and upper extremity pain</li> <li>• no evidence of disc herniation or radiculitis</li> </ul>	<ul style="list-style-type: none"> <li>• cervical disc herniation</li> <li>• radiculitis secondary to spinal stenosis without disc herniation</li> <li>• uncontrollable/unstable opioid use</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid</li> </ul>
<b>Manchikanti (2010)</b> <sup>125</sup> Effectiveness of Fluoroscopic	cervical interlaminar epidural	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• cervical disc herniation or radiculitis</li> <li>• chronic (<math>\geq 6</math> months) function-limiting neck and upper extremity pain</li> </ul>	<ul style="list-style-type: none"> <li>• previous cervical spine surgery</li> <li>• radiculitis secondary to spinal stenosis without disc herniation</li> <li>• uncontrollable/unstable opioid use</li> <li>• uncontrolled psychiatric disorder or acute/chronic medical illness</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics or steroid</li> </ul>
<b>Stav (1993)</b> <sup>193</sup>	cervical interlaminar epidural	<ul style="list-style-type: none"> <li>• chronic refractory cervicobrachialgia</li> </ul>	<ul style="list-style-type: none"> <li>• NR</li> </ul>
<b>Manchikanti (2008)</b> <sup>137*</sup> Cervical Medial Branch Blocks <b>Manchikanti, 2006</b> <sup>126</sup>	cervical medial branch block	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• chronic (<math>\geq 6</math> months) function-limiting neck pain</li> <li>• diagnosis of facet joint pain (used controlled facet joint nerve blocks)</li> <li>• failed conservative management (PT, chiropractic manipulation, exercises, drug therapy, bedrest)</li> <li>• willing to return for follow-ups</li> </ul>	<ul style="list-style-type: none"> <li>• surgical procedure within previous 3 months</li> <li>• disc-related pain with radicular symptoms based on radiologic testing, symptomatology, and neurologic examination</li> <li>• heavy opioid use</li> <li>• acute/uncontrolled medical illness</li> <li>• uncontrolled major depression/psychiatric disorders</li> <li>• conditions that could interfere with interpretation of outcome assessments</li> <li>• patients unable to assume the prone position</li> <li>• pregnant/lactating women</li> <li>• pts with history/potential for adverse reaction to anesthetics, steroid, or Sarapin</li> </ul>

<b>Barnsley, 1994<sup>15</sup></b>	cervical intraarticular	<ul style="list-style-type: none"> <li>• <math>\geq 18</math> yrs</li> <li>• chronic (<math>\geq 3</math> months) neck pain attributed to a motor vehicle accident</li> <li>• relief of pain on both diagnostic blocks</li> <li>• longer period of pain relief with bupivacaine than lidocaine block</li> <li>• inordinately prolonged response to diagnostic block (n = 6 patients)</li> </ul>	<ul style="list-style-type: none"> <li>• any response to diagnostic other than stated in inclusion criteria</li> </ul>
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MRI: magnetic resonance imaging

PT: physical therapy

\*Additional exclusion information provided by an earlier report of this study [Manchikanti, 2006].

**Appendix L. Efficacy data from RCTs: lumbar epidural injections**

Author (Year)	Study type  No. patients randomized (N) Diagnosis Duration of symptoms Mean age (range) Sex	Duration of f/u (% complete f/u rate)	Injection approach (guidance) Steroids used Diagnostic block Repeat injections (mean no. of injections) Cointerventions	Main results	Conflict of interest	LoE
<b>Manchikanti (2008, pt 2)</b> <sup>132</sup>	<b>RCT</b>  N = 120  LBP due to disc herniation and radiculitis  Chronic ( $\geq 6$ months)  Mean age ( $\pm$ SD): 47.1 $\pm$ 14.9* years  67% female*	3 months: 68% (82/120)  6 months: 64% (77/120)  12 months: 62% (74/120)  % patients with data carried forward† (steroid vs control):  3 months: 2% (1/42) vs 2% (1/42)  6 months: 7% (3/42) vs 10% (4/42)	Caudal epidural (fluoroscopy guidance)  <u>Steroids used:</u> Betamethasone (6 mg) <u>OR</u> methylprednisone (40 mg)  <u>Repeat injections:</u> as needed with increasing pain (mean: 3.8 $\pm$ 1.2 injections/year)  <u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)	<b>Caudal epidural steroid/saline/local anesthetic versus saline/local anesthetic injection (mean scores)</b>  (n = 42 per group, see info on % pts with data carried forward at each f/u)  <u>Pain</u> <ul style="list-style-type: none"> <li>• <b>Pain scores (NRS, 0 to 10 cm) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 7.9 <math>\pm</math> 1.0 versus 8.0 <math>\pm</math> 0.8 (ns)</li> <li>• 3 months: 3.4 <math>\pm</math> 1.7 versus 3.8 <math>\pm</math> 1.6 (ns)</li> <li>• 6 months: 3.5 <math>\pm</math> 1.7 versus 3.6 <math>\pm</math> 1.5 (ns)</li> <li>• 12 months: 3.5 <math>\pm</math> 1.8 versus 3.7 <math>\pm</math> 1.4 (ns)</li> </ul> </li> <li>• <b>Pain relief, <math>\geq 50\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 81% versus 81% (ns)</li> <li>• 6 months: 86% versus 86% (ns)</li> <li>• 12 months: 81% versus 79% (ns)</li> </ul> </li> </ul> <u>Function</u> <ul style="list-style-type: none"> <li>• <b>ODI (0-50 scale) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 28.5 <math>\pm</math> 4.4 versus 28.6 <math>\pm</math> 4.6 (ns)</li> <li>• 3 months: 13.8 <math>\pm</math> 6.3 versus 15.4 <math>\pm</math></li> </ul> </li> </ul>	None	I Ib

		<p>12 months: 10% (4/42) vs 14% (6/42)</p>		<p>6.8 (ns)</p> <ul style="list-style-type: none"> <li>• 6 months: 13.5 ± 6.7 versus 14.2 ± 6.7 (ns)</li> <li>• 12 months: 12.5 ± 6.4 versus 14.1 ± 6.9 (ns)</li> </ul> <p>• <b>Functional improvement, ≥ 40% (% patients):</b></p> <ul style="list-style-type: none"> <li>• 3 months: 79% versus 79% (ns)</li> <li>• 6 months: 86% versus 86% (ns)</li> <li>• 12 months: 91% versus 83% (ns)</li> </ul> <p><b><u>Opioid intake (morphine equivalents in mg)</u></b></p> <ul style="list-style-type: none"> <li>• Baseline: 45.6 ± 45.6 versus 48.7 ± 45.3 (ns)</li> <li>• 3 months: 27.4 ± 20.4 versus 28.7 ± 15.5 (ns)</li> <li>• 6 months: 26.7 ± 20.8 versus 28.5 ± 15.7 (ns)</li> <li>• 12 months: 27.2 ± 20.8 versus 28.6 ± 15.6 (ns)</li> </ul> <p><b><u>Employed (part-time or full-time) (% of patients eligible for employment)‡</u></b></p> <ul style="list-style-type: none"> <li>• Baseline: 53% (9/17) versus 50% (6/12) (<i>P</i> = NR)</li> <li>• 12 months: 94% (16/17) versus 83% (10/12) (<i>P</i> = NR)</li> </ul> <p><b><u>No. of injections/year</u></b></p> <ul style="list-style-type: none"> <li>• 12 months: 3.6 ± 1.1 versus 3.9 ± 1.3 (ns)</li> </ul> <p><b><u>Total relief (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• Injection #1: 6.1 ± 6.6 (n = 42) versus (n = 42) 5.1 ± 6.2 (<i>P</i> = NR)</li> <li>• after 2<sup>nd</sup> injection: (n = 41) 12.1 ± 16.9 versus (n = 40) 8.4 ± 5.8 (<i>P</i> = NR)</li> <li>• after 3<sup>rd</sup> injection: (n = 35) 13.1 ± 12.5 versus (n = 35) 12.1 ± 6.0 (<i>P</i> = NR)</li> </ul>		
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				<ul style="list-style-type: none"> <li>• after 4<sup>th</sup> injection: (n = 26) 11.2 ± 4.4 versus (n = 27) 11.6 ± 3.5 (<i>P</i> = NR)</li> <li>• after 5<sup>th</sup> injection: (n = 9) 14.9 ± 4.4 versus (n = 18) 11.9 ± 2.2 (<i>P</i> = NR)</li> <li>• after 12 months (mean): 35.9 ± 15.3 versus 35.2 ± 17.2 (<i>P</i> = NR)</li> </ul>		
<b>Manchikanti (2010)<sup>136</sup></b> Evaluation of the effectiveness	<b>RCT</b> N = 120  LBP due to disc herniation and radiculitis  Chronic (≥ 6 months)  Mean age (± SD): 42.0 ± 11.8* years  66% female§	3 months: 57% (68/120)  6 months: 53% (64/120)  12 months: 50% (60/120)  <hr/> % patients with data carried forward† (steroid vs control):  3 months: 0% (0/35) vs 6% (2/35)  6 months: 6% (2/35) vs 11% (4/35)  12 months: 9% (3/35) vs	Interlaminar epidural (fluoroscopy guidance); between L5 and S1 or one space below the disc herniation level  <u>Steroids used:</u> Betamethasone (6 mg)  <u>Repeat injections:</u> as needed with increasing pain (mean: 4.1 ± 1.1 injections/year)  <u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)	<b>Interlaminar epidural steroid/local anesthetic versus local anesthetic injection (mean scores)</b>  <b>(n = 35 per group, see info on % pts with data carried forward at each f/u)</b>  <u>Pain</u> <ul style="list-style-type: none"> <li>• <b>Pain scores (NRS, 0 to 10 cm) (mean ± SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 7.7 ± 0.9 versus 8.3 ± 1.0 (<i>P</i> = .015)</li> <li>• 3 months: 3.5 ± 1.1 versus 3.9 ± 1.2 (ns)</li> <li>• 6 months: 3.4 ± 1.0 versus 4.3 ± 1.3 (<i>P</i> = .001)</li> <li>• 12 months: 3.3 ± 1.2 versus 3.9 ± 1.3 (ns)</li> </ul> </li> <li>• <b>Pain relief, ≥ 50% (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 86% versus 83% (ns)</li> <li>• 6 months: 89% versus 63% (<i>P</i> &lt; .02)</li> <li>• 12 months: 86% versus 74% (ns)</li> </ul> </li> </ul> <u>Function</u> <ul style="list-style-type: none"> <li>• <b>ODI (0-50 scale) (mean ± SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 28.9 ± 5.4 versus 29.8 ± 4.6 (ns)</li> <li>• 3 months: 13.8 ± 4.6 versus 15.4 ± 5.2 (ns)</li> <li>• 6 months: 13.4 ± 4.5 versus 16.2 ± 5.4 (<i>P</i> = .019)</li> <li>• 12 months: 12.8 ± 4.4 versus 15.2 ±</li> </ul> </li> </ul>	None	IIb

		20% (7/35)		<p>5.5 (<math>P = .045</math>)</p> <ul style="list-style-type: none"> <li>• <b>Functional improvement, <math>\geq 50\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 80% versus 71% (ns)</li> <li>• 6 months: 83% versus 57% (<math>P &lt; .05</math>)</li> <li>• 12 months: 83% versus 69% (ns)</li> </ul> </li> </ul> <p><b><u>Opioid intake (morphine equivalents in mg)</u></b></p> <ul style="list-style-type: none"> <li>• Baseline: <math>57 \pm 58.5</math> versus <math>39 \pm 7.2</math> (ns)</li> <li>• 3 months: <math>40 \pm 36.1</math> versus <math>35 \pm 7.5</math> (ns)</li> <li>• 6 months: <math>38 \pm 34.5</math> versus <math>34 \pm 9.3</math> (ns)</li> <li>• 12 months: <math>35 \pm 35.6</math> versus <math>33 \pm 10.9</math> (ns)</li> </ul> <p><b><u>Employed (part-time or full-time) (% of patients eligible for employment)<sup>‡</sup></u></b></p> <ul style="list-style-type: none"> <li>• Baseline: 69% (11/16) versus 75% (9/12) (<math>P = \text{NR}</math>)</li> <li>• 12 months: 88% (14/16) versus 83% (10/12) (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>No. of injections/year</u></b></p> <ul style="list-style-type: none"> <li>• 12 months: <math>4.2 \pm 0.9</math> versus <math>3.9 \pm 1.3</math> (ns)</li> </ul> <p><b><u>Total relief (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• Injection #1: (<math>n = 35</math>) <math>5.1 \pm 3.5</math> versus (<math>n = 35</math>) <math>5.1 \pm 4.4</math> (<math>P = \text{NR}</math>)</li> <li>• after 2<sup>nd</sup> injection: (<math>n = 35</math>) <math>8.0 \pm 3.9</math> versus (<math>n = 32</math>) <math>8.5 \pm 4.3</math> (<math>P = \text{NR}</math>)</li> <li>• after 3<sup>rd</sup> injection: (<math>n = 32</math>) <math>11.9 \pm 2.2</math> versus (<math>n = 31</math>) <math>11.0 \pm 4.6</math> (<math>P = \text{NR}</math>)</li> <li>• after 4<sup>th</sup> injection: (<math>n = 30</math>) <math>14.1 \pm 7.7</math> versus (<math>n = 23</math>) <math>11.4 \pm 3.8</math> (<math>P = \text{NR}</math>)</li> <li>• after 5<sup>th</sup> injection: (<math>n = 14</math>) <math>12.6 \pm 0.9</math> versus (<math>n = 16</math>) <math>12.6 \pm 1.1</math> (<math>P =</math></li> </ul>	
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				<p>NR)</p> <ul style="list-style-type: none"> <li>after 12 months (mean): <math>40.2 \pm 12.9</math> versus <math>35.3 \pm 18.1</math> (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>Average relief per procedure (weeks)</u></b></p> <ul style="list-style-type: none"> <li><math>9.9 \pm 5.6</math> versus <math>9.2 \pm 4.8</math> (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>Average relief per procedure, 3<sup>rd</sup> procedure and after (weeks)</u></b></p> <ul style="list-style-type: none"> <li><math>12.9 \pm 5.1</math> versus <math>11.5 \pm 3.8</math> (<math>P = \text{NR}</math>)</li> </ul>		
<p><b>Manchikanti (2008, pt 1)<sup>118</sup></b></p>	<p><b>RCT</b></p> <p>N = 120</p> <p>LBP without disc herniation or radiculitis, based on controlled facet joint nerve blocks</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): <math>46.0 \pm 14.6^*</math> years</p> <p>60% female*</p>	<p>3 months: 59% (71/120)</p> <p>6 months: 57% (68/120)</p> <p>12 months: 52% (62/120)</p> <hr/> <p>% patients with data carried forward† (steroid vs control):</p> <p>3 months: 3% (1/36) vs 0% (0/36)</p> <p>6 months: 3% (1/36) vs 8% (3/36)</p> <p>12 months:</p>	<p>Caudal epidural (fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone (6 mg) <u>OR</u> methylprednisone (40 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: <math>3.8 \pm 1.2</math> injections/year)</p> <p><u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)</p>	<p><b>Caudal epidural steroid/saline/local anesthetic versus saline/local anesthetic injection (mean scores)</b></p> <p>(n = 36 per group, see info on % pts with data carried forward at each f/u)</p> <p><b><u>Pain</u></b></p> <ul style="list-style-type: none"> <li><b>Pain scores (NRS, 0 to 10 cm) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>Baseline: <math>7.9 \pm 1.1</math> versus <math>7.9 \pm 0.8</math> (ns)</li> <li>3 months: <math>3.7 \pm 1.4</math> versus <math>3.7 \pm 1.2</math> (ns)</li> <li>6 months: <math>3.8 \pm 1.3</math> versus <math>3.6 \pm 1.1</math> (ns)</li> <li>12 months: <math>3.9 \pm 1.6</math> versus <math>3.7 \pm 1.2</math> (ns)</li> </ul> </li> <li><b>Pain relief, <math>\geq 50\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>3 months: 78% versus 78% (ns)</li> <li>6 months: 75% versus 81% (ns)</li> <li>12 months: 72% versus 72% (ns)</li> </ul> </li> </ul> <p><b><u>Function</u></b></p> <ul style="list-style-type: none"> <li><b>ODI (0-50 scale) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>Baseline: <math>27.9 \pm 5.0</math> versus <math>26.9 \pm 5.2</math> (ns)</li> <li>3 months: <math>14.1 \pm 5.4</math> versus <math>13.8 \pm 4.8</math> (ns)</li> </ul> </li> </ul>	None	I Ib

		<p>8% (3/36) vs 19% (7/36)</p>		<ul style="list-style-type: none"> <li>• 6 months: <math>13.7 \pm 5.3</math> versus <math>13.3 \pm 5.2</math> (ns)</li> <li>• 12 months: <math>13.8 \pm 5.3</math> versus <math>13.1 \pm 4.9</math> (ns)</li> </ul> <p>• <b>Functional improvement, <math>\geq 40\%</math> (% patients):</b></p> <ul style="list-style-type: none"> <li>• 3 months: 81% versus 81% (ns)</li> <li>• 6 months: 81% versus 81% (ns)</li> <li>• 12 months: 81% versus 81% (ns)</li> </ul> <p><b><u>Opioid intake (morphine equivalents in mg)</u></b></p> <ul style="list-style-type: none"> <li>• Baseline: <math>46.4 \pm 23.8</math> versus <math>41.4 \pm 38.1</math> (ns)</li> <li>• 3 months: <math>34.7 \pm 22.8</math> versus <math>31.2 \pm 29.9</math> (ns)</li> <li>• 6 months: <math>38.5 \pm 38.1</math> versus <math>30.9 \pm 30.1</math> (ns)</li> <li>• 12 months: <math>35.3 \pm 22.6</math> versus <math>30.9 \pm 30.1</math> (ns)</li> </ul> <p><b><u>Employed (part-time or full-time) (% of patients eligible for employment)<sup>‡</sup></u></b></p> <ul style="list-style-type: none"> <li>• Baseline: 57% (8/14) versus 45% (5/11) (<math>P = \text{NR}</math>)</li> <li>• 12 months: 85% (11/13) versus 82% (9/11) (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>No. of injections/year</u></b></p> <ul style="list-style-type: none"> <li>• 12 months: <math>3.9 \pm 1.3</math> versus <math>3.6 \pm 1.1</math> (ns)</li> </ul> <p><b><u>Total relief (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• Injection #1: (n = 36) <math>4.6 \pm 4.0</math> versus (n = 36) <math>5.7 \pm 6.6</math> (<math>P = \text{NR}</math>)</li> <li>• after 2<sup>nd</sup> injection: (n = 33) <math>7.2 \pm 4.6</math> versus (n = 35) <math>9.3 \pm 7.2</math> (<math>P = \text{NR}</math>)</li> <li>• after 3<sup>rd</sup> injection: (n = 29) <math>10.1 \pm 4.0</math> versus (n = 30) <math>10.5 \pm 6.0</math> (<math>P = \text{NR}</math>)</li> <li>• after 4<sup>th</sup> injection: (n = 26) <math>10.6 \pm 4.1</math> versus (n = 21) <math>11.7 \pm 5.1</math> (<math>P =</math></li> </ul>		
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				<p>NR)</p> <ul style="list-style-type: none"> <li>• after 5<sup>th</sup> injection: (n = 14) 10.6 ± 3.9 versus (n = 8) 12.3 ± 1.4 (P = NR)</li> <li>• after 12 months (mean): 30.7 ± 17.94 versus 32.3 ± 16.93 (P = NR)</li> </ul>		
<p><b>Manchikanti (2010)<sup>116</sup></b> Preliminary Results of a Randomized</p>	<p><b>RCT</b></p> <p>N = 120</p> <p>LBP without disc herniation or radiculitis, based on controlled facet joint nerve blocks</p> <p>Chronic (≥ 6 months)</p> <p>Mean age (± SD): 41.8 ± 12.2* years</p> <p>67% female*</p>	<p>3 months: 57% (57/120)</p> <p>6 months: 53% (64/120)</p> <p>12 months: 49% (59/120)</p> <hr/> <p>% patients with data carried forward† (steroid vs control):</p> <p>3 months: 3% (1/35) vs 3% (1/35)</p> <p>6 months: 9% (3/35) vs 9% (3/35)</p> <p>12 months: 20% (7/35) vs 11% (4/35)</p>	<p>Interlaminar epidural (fluoroscopy guidance); between L5 and S1 or at higher level</p> <p><u>Steroids used:</u> Betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: 3.9 ± 1.1 injections/year)</p> <p><u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)</p>	<p><b>Interlaminar epidural steroid/local anesthetic versus local anesthetic injection (mean scores)</b></p> <p>(n = 35 per group, see info on % pts with data carried forward at each f/u)</p> <p><u>Pain</u></p> <ul style="list-style-type: none"> <li>• <b>Pain scores (NRS, 0 to 10 cm) (mean ± SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 7.6 ± 0.9 versus 8.1 ± 0.9 (P = .010)</li> <li>• 3 months: 3.4 ± 1.1 versus 3.7 ± 1.0 (ns)</li> <li>• 6 months: 3.5 ± 1.2 versus 4.1 ± 1.2 (ns)</li> <li>• 12 months: 3.8 ± 1.3 versus 3.9 ± 1.2 (ns)</li> </ul> </li> <li>• <b>Pain relief, ≥ 50% (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 86% versus 77% (ns)</li> <li>• 6 months: 86% versus 80% (ns)</li> <li>• 12 months: 80% versus 80% (ns)</li> </ul> </li> </ul> <p><u>Function</u></p> <ul style="list-style-type: none"> <li>• <b>ODI (0-50 scale) (mean ± SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 28.8 ± 5.1 versus 30.2 ± 3.8 (ns)</li> <li>• 3 months: 13.9 ± 4.8 versus 14.6 ± 4.1 (ns)</li> <li>• 6 months: 14.4 ± 4.9 versus 15.7 ± 5.1 (ns)</li> <li>• 12 months: 15.9 ± 6.9 versus 15.0 ± 5.2 (ns)</li> </ul> </li> </ul>	None	I Ib

				<ul style="list-style-type: none"> <li>• <b>Functional improvement, <math>\geq 50\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 80% versus 83% (ns)</li> <li>• 6 months: 69% versus 69% (ns)</li> <li>• 12 months: 60% versus 71% (ns)</li> </ul> </li> <li>• <b><u>Opioid intake (morphine equivalents in mg)</u></b> <ul style="list-style-type: none"> <li>• Baseline: <math>61 \pm 71.5</math> versus <math>52 \pm 61.2</math> (ns)</li> <li>• 3 months: <math>49 \pm 59.8</math> versus <math>39 \pm 29.3</math> (ns)</li> <li>• 6 months: <math>43 \pm 43.7</math> versus <math>42 \pm 32.3</math> (ns)</li> <li>• 12 months: <math>42 \pm 44.2</math> versus <math>41 \pm 32.9</math> (ns)</li> </ul> </li> <li>• <b><u>Employed (part-time or full-time) (% of patients eligible for employment)<sup>‡</sup></u></b> <ul style="list-style-type: none"> <li>• Baseline: 67% (8/12) versus 55% (6/11) (<math>P = \text{NR}</math>)</li> <li>• 12 months: 83% (10/12) versus 64% (7/11) (<math>P = \text{NR}</math>)</li> </ul> </li> <li>• <b><u>No. of injections/year</u></b> <ul style="list-style-type: none"> <li>• 12 months: <math>3.8 \pm 1.1</math> versus <math>3.9 \pm 1.1</math> (ns)</li> </ul> </li> <li>• <b><u>Total relief (weeks)</u></b> <ul style="list-style-type: none"> <li>• Injection #1: (n = 35) <math>5.6 \pm 4.0</math> versus (n = 35) <math>6.2 \pm 4.3</math> (<math>P = \text{NR}</math>)</li> <li>• after 2<sup>nd</sup> injection: (n = 33) <math>8.8 \pm 3.5</math> versus (n = 33) <math>9.6 \pm 3.3</math> (<math>P = \text{NR}</math>)</li> <li>• after 3<sup>rd</sup> injection: (n = 30) <math>10.2 \pm 4.1</math> versus (n = 33) <math>11.6 \pm 3.0</math> (<math>P = \text{NR}</math>)</li> <li>• after 4<sup>th</sup> injection: (n = 24) <math>11.3 \pm 3.3</math> versus (n = 23) <math>11.9 \pm 4.4</math> (<math>P = \text{NR}</math>)</li> <li>• after 5<sup>th</sup> injection: (n = 10) <math>12.5 \pm 0.8</math> versus (n = 11) <math>12.5 \pm 1.3</math> (<math>P = \text{NR}</math>)</li> </ul> </li> </ul>		
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				<ul style="list-style-type: none"> <li>after 12 months (mean): <math>33.9 \pm 16.0</math> versus <math>37.4 \pm 14.7</math> (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>Average relief per procedure (weeks)</u></b></p> <ul style="list-style-type: none"> <li><math>9.0 \pm 4.3</math> versus <math>9.8 \pm 4.2</math> (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>Average relief per procedure, 3<sup>rd</sup> procedure and after (weeks)</u></b></p> <ul style="list-style-type: none"> <li><math>11.0 \pm 3.5</math> versus <math>11.9 \pm 3.3</math> (<math>P = \text{NR}</math>)</li> </ul>		
<b>Manchikanti (2008, pt 4)<sup>115</sup></b>	<p><b>RCT</b></p> <p>N = 61</p> <p>LBP due to spinal stenosis with radiculitis</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): <math>60.4 \pm 15.8^*</math> years</p> <p>70% female*</p>	<p>3 months: 59% (36/61)</p> <p>6 months: 49% (30/61)</p> <p>12 months: 46% (28/61)</p> <hr/> <p>% patients with data carried forward† (steroid vs control):</p> <p>3 months: 15% (3/20) vs 5% (1/20)</p> <p>6 months: 25% (5/20) vs 25% (5/20)</p> <p>12 months: 25% (5/20) vs 35% (7/20)</p>	<p>Caudal epidural (fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: <math>3.0 \pm 1.2</math> injections/year)</p> <p><u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)</p>	<p><b>Caudal epidural steroid/saline/local anesthetic versus saline/local anesthetic injection (mean scores)</b></p> <p>(n = 20 per group, see info on % pts with data carried forward at each f/u)</p> <p><b><u>Pain</u></b></p> <ul style="list-style-type: none"> <li><b>Pain scores (NRS, 0 to 10 cm) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>Baseline: <math>7.5 \pm 1.1</math> versus <math>8.1 \pm 1.0</math> (ns)</li> <li>3 months: <math>4.2 \pm 2.4</math> versus <math>4.2 \pm 2.2</math> (ns)</li> <li><del>6 months: <math>4.1 \pm 2.2</math> versus <math>4.0 \pm 2.2</math> (ns) †</del></li> <li><del>12 months: <math>4.1 \pm 2.5</math> versus <math>3.8 \pm 2.0</math> (ns) †</del></li> </ul> </li> <li><b>Pain relief, <math>\geq 50\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>3 months: 50% versus 65% (ns)</li> <li><del>6 months: 60% versus 70% (ns) †</del></li> <li><del>12 months: 55% versus 65% (ns) †</del></li> </ul> </li> </ul> <p><b><u>Function</u></b></p> <ul style="list-style-type: none"> <li><b>ODI (0-50 scale) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>Baseline: <math>26.1 \pm 4.6</math> versus <math>28.4 \pm 4.5</math> (ns)</li> <li>3 months: <math>16.4 \pm 8.3</math> versus <math>16.4 \pm 7.5</math> (ns)</li> <li><del>6 months: <math>15.5 \pm 8.4</math> versus <math>15.4 \pm 7.8</math> (ns) †</del></li> </ul> </li> </ul>	None	I Ib

				<ul style="list-style-type: none"> <li>• 12 months: 15.8 ± 8.6 versus 14.3 ± 8.5 (ns) †</li> <li>• <b>Functional improvement, ≥ 40% (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 50% versus 65% (ns)</li> <li>• 6 months: 60% versus 75% (ns) †</li> <li>• 12 months: 55% versus 80% (ns) †</li> </ul> </li> <li>• <b><u>Opioid intake (morphine equivalents in mg/day)</u></b> <ul style="list-style-type: none"> <li>• Baseline: 33.3 ± 36.9 versus 45.9 ± 54.8 (ns)</li> <li>• 3 months: 21.2 ± 18.9 versus 35.6 ± 53.1 (ns)</li> <li>• 6 months: 20.5 ± 19.1 versus 35.1 ± 53.3 (ns) †</li> <li>• 12 months: 20.5 ± 19.1 versus 35.1 ± 53.3 (ns) †</li> </ul> </li> <li>• <b><u>Employed (part-time or full-time) (% of patients eligible for employment)†</u></b> <ul style="list-style-type: none"> <li>• Baseline: 40% (2/5) versus 33% (1/3) (<i>P</i> = NR)</li> <li>• 12 months: 60% (3/5) versus 67% (2/3) (<i>P</i> = NR)†</li> </ul> </li> <li>• <b><u>No. of injections/year</u></b> <ul style="list-style-type: none"> <li>• 12 months: 2.6 ± 1.4 versus 3.4 ± 1.3 (ns) †</li> </ul> </li> <li>• <b><u>Total relief (weeks)</u></b> <ul style="list-style-type: none"> <li>• Injection #1: (n = 20) 3.7 ± 5.5 versus (n = 20) 6.2 ± 8.5 (<i>P</i> = NR)</li> <li>• after 2<sup>nd</sup> injection: (n = 15) 12.3 ± 3.8 versus (n = 20) 9.1 ± 7.9 (<i>P</i> = NR)</li> <li>• after 3<sup>rd</sup> injection: (n = 9) 13.3 ± 5.1 versus (n = 13) 11.7 ± 6.0 (<i>P</i> = NR)</li> <li>• after 4<sup>th</sup> injection: (n = 7) 12.6 ± 1.1 versus (n = 10) 10.2 ± 4.1 (<i>P</i> = NR)</li> <li>• after 5<sup>th</sup> injection: (n = 4) 14.8 ± 4.9 versus (n = 5) 11.6 ± 2.0 (<i>P</i> = NR)</li> </ul> </li> </ul>		
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				<ul style="list-style-type: none"> <li>after 12 months (mean): <math>23.1 \pm 21.4</math> versus <math>30.3 \pm 19.5</math> (<math>P = \text{NR}</math>)</li> </ul>		
<p><b>Sayegh (2009)<sup>176</sup></b></p>	<p><b>RCT</b></p> <p>N = 183</p> <p>LBP with disc herniation or radiculitis, based on MRI scan</p> <p>Chronic (<math>\geq 1</math> month)</p> <p>Mean age (<math>\pm</math> SD): <math>49.3 \pm 15.6</math> years</p> <p>33% female</p>	<p>1 week: (100% f/u; 183/183)</p> <p>1 month: (95% f/u; 174/183)</p> <p>6 months: (84% f/u; 153/183)</p> <p>12 months: (83% f/u; 151/183)</p>	<p>Caudal epidural (without fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone dipropionate (1 mL) and betamethasone phosphate ((2+5) mg/dL)</p> <p><u>Repeat injections:</u> as needed if ODI and SLR test did not improve; 28% (51/183) patients received 2<sup>nd</sup> injection; (mean injections/year NR)</p> <p><u>Cointerventions:</u> Pts allowed to receive paracetamol during first 4 weeks of study, but not non-steroid anti-inflammatory meds</p>	<p><b>Caudal epidural steroid/local anesthetic (n = 93) versus water/local anesthetic injection (n = 90) (mean scores)</b></p> <p><b>Function</b></p> <ul style="list-style-type: none"> <li><b>ODI (0-50 scale) (mean <math>\pm</math> SD)**:</b></li> <li>Baseline: <math>38.5 \pm 2.6</math> versus <math>38.5 \pm 2.7</math> (ns)</li> <li>1 week: <math>12.1 \pm 13.1</math> versus <math>29.9 \pm 6.2</math> (<math>P = .000</math>)</li> <li>1 month: <math>8.7 \pm 11.9</math> versus <math>23.5 \pm 9.6</math> (<math>P = .000</math>)</li> <li>6 months: <math>5.8 \pm 8.6</math> versus <math>13.6 \pm 10.5</math> (<math>P = .000</math>)</li> <li>12 months: <math>4.9 \pm 7.1</math> versus <math>13.0 \pm 10.1</math> (<math>P = .000</math>)</li> <li><b>“Positive” SLR (<math>&lt; 60^\circ</math>) (% patients)**:</b></li> <li>Baseline: 63% versus 56% (ns)</li> <li>1 week: 38% versus 47% (ns)</li> <li>1 month: 24% versus 46% (<math>P = .002</math>)</li> <li>6 months: 6% versus 13% (ns)</li> <li>12 months: 2% versus 9% (ns)</li> </ul>	None	I Ib
<p><b>Manchikanti (2008, pt 3)<sup>133</sup></b></p>	<p><b>RCT</b></p> <p>N = 68</p> <p>LBP due to post lumbar surgery syndrome</p>	<p>3 months: 54% (37/68)</p> <p>6 months: 47% (32/68)</p> <p>12 months: 38%</p>	<p>Caudal epidural (fluoroscopy guidance)</p> <p><u>Steroids used:</u> betamethasone (6 mg)</p>	<p><b>Caudal epidural steroid/saline/local anesthetic versus saline/local anesthetic injection (mean scores)</b></p> <p>(n = 20 per group, see info on % pts with data carried forward at each f/u.)</p> <p><b>Pain</b></p>	None	I Ib

	<p>Chronic (<math>\geq 6</math> months after previous lumbar surgery)</p> <p>Mean age (<math>\pm</math> SD): 53.1 <math>\pm</math> 13.0* years</p> <p>55% female*</p>	<p>(26/68)</p> <hr/> <p>% patients with data carried forward† (steroid vs control):</p> <p>3 months: 10% (2/20) vs 5% (1/20)</p> <p>6 months: 25% (5/20) vs 15% (3/20)</p> <p>12 months: 35% (7/20) vs 35% (7/20)</p>	<p><u>Repeat injections:</u> as needed with increasing pain (mean: 3.4 <math>\pm</math> 1.3 injections/year)</p> <p><u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• <b>Pain scores (NRS, 0 to 10 cm) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 7.9 <math>\pm</math> 0.9 versus 8.0 <math>\pm</math> 1.1 (ns)</li> <li>• 3 months: 4.1 <math>\pm</math> 1.5 versus 3.8 <math>\pm</math> 1.7 (ns)</li> <li>• <del>6 months: 4.1 <math>\pm</math> 1.6 versus 4.3 <math>\pm</math> 2.0 (ns) †</del></li> <li>• <del>12 months: 4.4 <math>\pm</math> 1.5 versus 4.2 <math>\pm</math> 2.0 (ns) †</del></li> </ul> </li> <li>• <b>Pain relief, <math>\geq 50\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 65% versus 70% (ns)</li> <li>• <del>6 months: 60% versus 60% (ns) †</del></li> <li>• <del>12 months: 60% versus 65% (ns) †</del></li> </ul> </li> </ul> <p><u>Function</u></p> <ul style="list-style-type: none"> <li>• <b>ODI (0-50 scale) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 27.4 <math>\pm</math> 5.1 versus 28.9 <math>\pm</math> 5.2 (ns)</li> <li>• 3 months: 15.7 <math>\pm</math> 6.6 versus 15.8 <math>\pm</math> 5.7 (ns)</li> <li>• <del>6 months: 15.3 <math>\pm</math> 7.3 versus 16.3 <math>\pm</math> 6.8 (ns) †</del></li> <li>• <del>12 months: 15.9 <math>\pm</math> 7.2 versus 15.8 <math>\pm</math> 7.1 (ns) †</del></li> </ul> </li> <li>• <b>Functional improvement, <math>\geq 40\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 70% versus 70% (ns)</li> <li>• <del>6 months: 65% versus 65% (ns) †</del></li> <li>• <del>12 months: 55% versus 70% (ns) †</del></li> </ul> </li> </ul> <p><u>Opioid intake (morphine equivalents in mg/day)</u></p> <ul style="list-style-type: none"> <li>• Baseline: 59.1 <math>\pm</math> 44.4 versus 46.9 <math>\pm</math> 34.6 (ns)</li> <li>• 3 months: 40.4 <math>\pm</math> 38.3 versus 32.5 <math>\pm</math> 22.3 (ns)</li> <li>• <del>6 months: 39.8 <math>\pm</math> 38.8 versus 39.2 <math>\pm</math> 47.2 (ns) †</del></li> <li>• <del>12 months: 38.8 <math>\pm</math> 39.1 versus 33.0</del></li> </ul>		
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				$\pm 22.6$ (ns) † <u>Employed (part-time or full-time) (% of patients eligible for employment)†</u> <ul style="list-style-type: none"> <li>Baseline: 25% (2/8) versus 50% (2/4) (<math>P = \text{NR}</math>)</li> <li>12 months: 25% (2/8) versus 75% (3/4) (<math>P = \text{NR}</math>)†</li> </ul> <u>No. of injections/year</u> <ul style="list-style-type: none"> <li>12 months: <math>3.4 \pm 1.3</math> versus <math>3.4 \pm 1.4</math> (ns) †</li> </ul> <u>Total relief (weeks)</u> <ul style="list-style-type: none"> <li>Injection #1: (n = 20) <math>2.8 \pm 1.6</math> versus (n = 20) <math>4.8 \pm 3.6</math> (<math>P = .03</math>)</li> <li>after 2<sup>nd</sup> injection: (n = 18) <math>7.3 \pm 3.8</math> versus (n = 18) <math>8.9 \pm 8.1</math> (ns)</li> <li>after 3<sup>rd</sup> injection: (n = 15) <math>11.2 \pm 5.7</math> versus (n = 14) <math>11.6 \pm 8.8</math> (ns)</li> <li>after 4<sup>th</sup> injection: (n = 11) <math>11.3 \pm 3.6</math> versus (n = 9) <math>14.1 \pm 3.0</math> (ns)</li> <li>after 5<sup>th</sup> injection: (n = 6) <math>13.7 \pm 4.4</math> versus (n = 7) <math>13.0 \pm 0</math> (ns)</li> <li>after 12 months (mean): <math>26.2 \pm 18.3</math> versus <math>31.7 \pm 19.1</math> (ns)</li> </ul>		
<b>Manchikanti (2009)<sup>117</sup></b> Preliminary Results of a Comparative	<b>RCT</b> N = 82 LBP due to spinal stenosis with radiculitis Chronic ( $\geq 6$ months) Mean age ( $\pm$ SD): $61.5 \pm 13.2^*$ years 58% female*	3 months: 61% (50/82) 6 months: 49% (40/82) 12 months: 39% (32/82) % patients with data carried forward† (steroid vs	Percutaneous epidural adhesiolysis (fluoroscopy and lumbar epidurogram guidance)†† Steroids used (both treatment and control groups): betamethasone (6 mg) Repeat injections:	<b>Caudal epidural injection (steroid/normal saline/local anesthetic injection) versus percutaneous epidural adhesiolysis (steroid/10% saline/local anesthetic)†† (mean scores)</b> (n = 25 per group, see info on % pts with data carried forward at each f/u.) <b>Pain</b> <ul style="list-style-type: none"> <li>Pain scores (NRS, 0 to 10 cm) (mean <math>\pm</math> SD):               <ul style="list-style-type: none"> <li>Baseline: <math>8.0 \pm 1.1</math> versus <math>7.8 \pm 0.9</math> (ns)</li> <li>3 months: <math>5.4 \pm 1.6</math> versus <math>3.6 \pm 1.2</math></li> </ul> </li> </ul>	None	I Ib

		<p>control):</p> <p>3 months: 0% (0/25) vs 0% (0/25)</p> <p>6 months: 40% (10/25) vs 0% (0/25)</p> <p>12 months: 72% (18/25) vs 0% (0/25)</p>	<p>as needed with increasing pain (mean: <math>2.7 \pm 0.9</math> injections/year)</p> <p><u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)</p>	<p>(<math>P = .000</math>)</p> <ul style="list-style-type: none"> <li>• <del>6 months: <math>6.0 \pm 1.2</math> versus <math>3.8 \pm 1.2</math></del> (<math>P = .000</math>)<sup>†</sup></li> <li>• <del>12 months: <math>6.2 \pm 0.9</math> versus <math>3.9 \pm 1.2</math></del> (<math>P = .000</math>)<sup>†</sup></li> <li>• <b>Pain relief, <math>\geq 50\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 28% versus 80% (<math>P = \text{NR}</math>)</li> <li>• <del>6 months: 12% versus 80%</del> (<math>P = \text{NR}</math>)<sup>†</sup></li> <li>• <del>12 months: 4% versus 76%</del> (<math>P &lt; .05</math>)<sup>††</sup></li> </ul> </li> </ul> <p><u>Function</u></p> <ul style="list-style-type: none"> <li>• <b>ODI (0-50 scale) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>• Baseline: <math>30.2 \pm 4.9</math> versus <math>30.6 \pm 4.1</math> (ns)</li> <li>• 3 months: <math>23.3 \pm 6.2</math> versus <math>15.6 \pm 5.3</math> (<math>P = .000</math>)</li> <li>• <del>6 months: <math>25.2 \pm 4.5</math> versus <math>15.8 \pm 4.4</math></del> (<math>P = .000</math>)<sup>†</sup></li> <li>• <del>12 months: <math>25.4 \pm 4.4</math> versus <math>15.6 \pm 4.7</math></del> (<math>P = .000</math>)<sup>†</sup></li> </ul> </li> <li>• <b>Functional improvement, <math>\geq 40\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 24% versus 80% (<math>P = \text{NR}</math>)</li> <li>• <del>6 months: 8% versus 76%</del> (<math>P = \text{NR}</math>)<sup>†</sup></li> <li>• <del>12 months: 0% versus 80%</del> (<math>P = \text{NR}</math>)<sup>†</sup></li> </ul> </li> </ul> <p><u>Opioid intake (morphine equivalents in mg/day)</u></p> <ul style="list-style-type: none"> <li>• Baseline: <math>42 \pm 22.9</math> versus <math>38 \pm 21.6</math> (ns)</li> <li>• 3 months: <math>35 \pm 12.4</math> versus <math>32 \pm 13.8</math> (ns)</li> <li>• <del>6 months: <math>35 \pm 12.4</math> versus <math>32 \pm</math></del></li> </ul>		
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				<p>14.1(ns) †</p> <ul style="list-style-type: none"> <li>12 months: 35 ± 12.4 versus 32 ± 13.9 (ns) †</li> </ul> <p><b><u>Employed (part-time or full-time) (% of patients eligible for employment)†</u></b></p> <ul style="list-style-type: none"> <li>Baseline: 75% (3/4) versus 50% (1/2) (P = NR)</li> <li>12 months: 50% (2/4) versus 100% (2/2) (P = NR)†</li> </ul> <p><b><u>No. of injections/year</u></b></p> <ul style="list-style-type: none"> <li>12 months: 1.8 ± 0.9 versus 3.5 ± 1.0 (P &lt; .05) †</li> </ul> <p><b><u>Total relief in back pain (weeks)</u></b></p> <ul style="list-style-type: none"> <li>Injection #1: (n = 25) 2.9 ± 3.9 versus (n = 25) 9.6 ± 4.8 (ns)</li> <li>after 2<sup>nd</sup> injection: (n = 15) 3.3 ± 3.3 versus (n = 23) 14.9 ± 20.6 (ns)</li> <li>after 3<sup>rd</sup> injection: (n = 5) 3.2 ± 3.7 versus (n = 20) 12.8 ± 1.0 (P = ns)</li> <li>after 4<sup>th</sup> injection: (n = 1) 9.0 versus (n = 19) 12.4 ± 1.3 (P = ns)</li> <li>after 12 months (mean): 5.9 ± 8.9 versus 43.0 ± 22.9 (P &lt; .05) †</li> </ul> <p><b><u>Total relief in leg pain (weeks)</u></b></p> <ul style="list-style-type: none"> <li>Injection #1: (n = 23) 2.8 ± 4.1 versus (n = 24) 10.1 ± 4.3 (ns)</li> <li>after 2<sup>nd</sup> injection: (n = 15) 3.1 ± 3.4 versus (n = 22) 15.8 ± 20.8 (ns)</li> <li>after 3<sup>rd</sup> injection: (n = 5) 3.2 ± 3.7 versus (n = 20) 12.3 ± 2.6 (P = ns)</li> <li>after 4<sup>th</sup> injection: (n = 1) 9.0 (n = 19) versus 11.7 ± 3.1 (P = ns)</li> <li>after 12 months (mean): 6.0 ± 9.3 versus 44.1 ± 21.9 (P &lt; .05) †</li> </ul> <p><b><u>Average relief in back pain per procedure (weeks)</u></b></p> <ul style="list-style-type: none"> <li>3.2 ± 3.7 versus 12.3 ± 10.9 (P &lt; .05)</li> </ul>	
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				<u>Average relief in leg pain per procedure (weeks)</u> • $3.1 \pm 3.8$ versus $12.5 \pm 11.0$ ( $P < .05$ )		
<b>Manchikanti (2009)<sup>134</sup>A</b> Comparative Effectiveness Evaluation	<b>RCT</b>  N = 180  LBP due to post lumbar surgery syndrome  Chronic ( $\geq 6$ months after previous lumbar surgery)  Mean age ( $\pm$ SD): $52 \pm 13.2^*$ years  58% female*	3 months: 67% (120/180)  6 months: 61% (109/180)  12 months: 41% (74/180)  % patients with data carried forward† (steroid vs control):  3 months: 0% (0/60) vs 0% (0/60)  6 months: 40% (10/60) vs 2% (1/60)  12 months: 72% (43/60) vs 5% (3/60)	Percutaneous epidural adhesiolysis (fluoroscopy and lumbar epidurogram guidance)††  Steroids used (both treatment and control groups): betamethasone (6 mg)  <u>Repeat injections:</u> as needed with increasing pain after at least 3 months (mean: $2.9 \pm 1.1$ injections/year)  <u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)	<b>Caudal epidural injection (steroid/normal saline/local anesthetic injection) versus percutaneous epidural adhesiolysis (steroid/10% saline/local anesthetic)†† (mean scores)</b>  (n = 60 per group, see info on % pts with data carried forward at each f/u.)  <u>Pain</u> • <b>Pain scores (NRS, 0 to 10 cm) (mean <math>\pm</math> SD):</b> • Baseline: $7.9 \pm 0.8$ versus $8.1 \pm 0.8$ (ns) • 3 months: $4.9 \pm 1.6$ versus $3.4 \pm 0.8$ ( $P = .000$ ) • <del>6 months: <math>5.8 \pm 1.5</math> versus <math>3.7 \pm 1.1</math> (<math>P = .000</math>)</del> † • <del>12 months: <math>6.1 \pm 1.4</math> versus <math>4.0 \pm 1.2</math> (<math>P = .000</math>)</del> † • <b>Pain relief, <math>\geq 50\%</math> (% patients):</b> • 3 months: 35% versus 90% ( $P < .05$ ) • <del>6 months: 18% versus 85% (<math>P &lt; .05</math>)</del> † • <del>12 months: 12% versus 73% (<math>P &lt; .05</math>)</del> † <u>Function</u> • <b>ODI (0-50 scale) (mean <math>\pm</math> SD):</b> • Baseline: $28.6 \pm 4.1$ versus $31.2 \pm 4.1$ ( $P = .001$ ) • 3 months: $20.2 \pm 6.6$ versus $15.2 \pm 4.1$ ( $P = .000$ ) • <del>6 months: <math>22.3 \pm 6.1</math> versus <math>15.2 \pm 5.2</math> (<math>P = .000</math>)</del> † • <del>12 months: <math>23.3 \pm 5.8</math> versus <math>15.8 \pm</math></del>	None	I Ib

				<p>5.6 (<math>P = .000</math>) †</p> <ul style="list-style-type: none"> <li>• <b>Functional improvement, <math>\geq 40\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 37% versus 92% (<math>P = \text{NR}</math>)</li> <li>• 6 months: 25% versus 88% (<math>P = \text{NR}</math>) †</li> <li>• 12 months: 13% versus 77% (<math>P = \text{NR}</math>) †</li> </ul> </li> </ul> <p><b><u>Opioid intake (morphine equivalents in mg/day)</u></b></p> <ul style="list-style-type: none"> <li>• Baseline: <math>41 \pm 21.8</math> versus <math>64 \pm 45.1</math> (<math>P = .001</math>)</li> <li>• 3 months: <math>42 \pm 28.6</math> versus <math>42 \pm 28.9</math> (ns)</li> <li>• 6 months: <math>47 \pm 42.4</math> versus <math>49 \pm 42.3</math> (ns) †</li> <li>• 12 months: <math>40 \pm 29.2</math> versus <math>41 \pm 28.6</math> (ns) †</li> </ul> <p><b><u>Employed (part-time or full-time) (% of patients eligible for employment)‡</u></b></p> <ul style="list-style-type: none"> <li>• Baseline: 75% (9/12) versus 100% (5/5) (<math>P = \text{NR}</math>)</li> <li>• 12 months: 75% (9/12) versus 100% (5/5) (<math>P = \text{NR}</math>) †</li> </ul> <p><b><u>No. of injections/year</u></b></p> <ul style="list-style-type: none"> <li>• 12 months: <math>2.2 \pm 1.1</math> versus <math>3.5 \pm 1.0</math> (<math>P &lt; .05</math>) ††</li> </ul> <p><b><u>Total relief in back pain (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• Injection #1: (n = 60) <math>4.8 \pm 4.3</math> versus (n = 60) <math>10.7 \pm 3.8</math> (<math>P &lt; .05</math>)</li> <li>• after 2<sup>nd</sup> injection: (n = 41) <math>6.3 \pm 4.5</math> versus (n = 56) <math>11.9 \pm 3.7</math> (<math>P &lt; .05</math>)</li> <li>• after 3<sup>rd</sup> injection: (n = 23) <math>6.7 \pm 4.6</math> versus (n = 52) <math>11.9 \pm 2.8</math> (<math>P &lt; .05</math>)</li> <li>• after 4<sup>th</sup> injection: (n = 10) <math>8.9 \pm 3.8</math> versus (n = 44) <math>12.5 \pm 2.7</math> (<math>P &lt; .05</math>)</li> <li>• after 12 months (mean): (n = 60)</li> </ul>	
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				<p>13.1 ± 14.2 versus (n = 60) 41.2 ± 14.7 (<math>P &lt; .05</math>) †</p> <p><b><u>Total relief in leg pain (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• Injection #1: (n = 59) 5.0 ± 4.4 versus (n = 58) 10.3 ± 4.1 (<math>P &lt; .05</math>)</li> <li>• after 2<sup>nd</sup> injection: (n = 40) 6.6 ± 4.4 versus (n = 54) 11.9 ± 3.8 (<math>P &lt; .05</math>)</li> <li>• after 3<sup>rd</sup> injection: (n = 23) 6.7 ± 4.6 versus (n = 50) 12.0 ± 2.8 (<math>P &lt; .05</math>)</li> <li>• after 4<sup>th</sup> injection: (n = 10) 8.9 ± 3.8 versus (n = 39) 12.5 ± 2.9 (<math>P &lt; .05</math>)</li> <li>• after 12 months (mean): (n = 59) 13.6 ± 14.1 versus (n = 58) 40.7 ± 15.3 (<math>P &lt; .05</math>) †</li> </ul> <p><b><u>Average relief in back pain per procedure (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• 5.9 ± 4.5 versus 11.7 ± 3.4 (<math>P &lt; .05</math>)</li> </ul> <p><b><u>Average relief in leg pain per procedure (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• 6.1 ± 4.5 versus 11.6 ± 3.5 (<math>P &lt; .05</math>)</li> </ul>		
Koc (2009) <sup>99</sup>	<p><b>RCT</b></p> <p>N = 33</p> <p>LBP due to spinal stenosis</p> <p>Chronic (mean duration of symptoms: 5.4 ± 5.6 years)*</p> <p>Mean age (± SD): 59 ± 10.8* years</p> <p>72% female*</p>	<p>2 wks, and 1, 3 months (% f/u: NR) 6 months(88% f/u; 29/33)</p>	<p>Interlaminar epidural (through the most stenotic level under fluoroscopy guidance)</p> <p><u>Steroids used</u> triamcinolone acetate (60 mg)</p> <p><u>Repeat injections:</u> (mean injections/year NR)</p> <p><u>Cointerventions:</u> all patients performed home-based</p>	<p><b>Interlaminar epidural steroid/local anesthetic (n = 10) versus physical therapy (n = 10) versus control (n = 9)††</b> (mean scores)</p> <p><b><u>Pain</u></b></p> <ul style="list-style-type: none"> <li>• <b>Pain scores (VAS, 0 to 100 mm) (mean):</b> <ul style="list-style-type: none"> <li>• Baseline: 53 versus 55 versus 58 (ns)</li> <li>• 2 weeks: 21 versus 32 versus 56 (<math>P = .008</math> percent change in steroid versus control)</li> <li>• 1 month: 28 versus 35 versus 36 (ns)</li> <li>• 3 months: 23 versus 24 versus 38 (ns)</li> <li>• 6 months: 26 versus 22 versus 33 (ns)</li> </ul> </li> </ul>	None	Iib

			therapeutic exercise program and received oral diclofenac sodium, 2 doses/day/2 weeks	<p><b><u>Function</u></b></p> <ul style="list-style-type: none"> <li>• <b>RMDI (0-24 scale) (mean):</b> <ul style="list-style-type: none"> <li>• Baseline: 18 versus 19 versus 15 (ns)</li> <li>• 2 weeks: 8 versus 12 versus 12 (<math>P = .007</math>: percent change in steroid versus control)</li> <li>• 1 month: 13 versus 14 versus 11 (ns)</li> <li>• 3 months: 11 versus 11 versus 10 (ns)</li> <li>• 6 months: 13 versus 12 versus 9 (ns)</li> </ul> </li> </ul> <p><b><u>Quality of Life</u></b></p> <ul style="list-style-type: none"> <li>• <b>NHP: VAS score (median percent change)</b> <ul style="list-style-type: none"> <li>• Baseline: 56.3 versus 54.1 versus 58.6 (ns)</li> <li>• 2 weeks: 7.3 versus 19.4 versus 33.0 (ns)</li> <li>• 1 month: 36.2 versus 31.2 versus 20.1 (ns)</li> <li>• 3 months: 20.5 versus 18.2 versus 27.7 (ns)</li> <li>• 6 months: 23.0 versus 23.2 versus 20.1 (ns)</li> </ul> </li> <li>• <b>NHP: Physical mobility score (median percent change)</b> <ul style="list-style-type: none"> <li>• Baseline: 41.8 versus 41.8 versus 41.8 (ns)</li> <li>• 2 weeks: 21.9 versus 31.2 versus 31.2 (<math>P = .004</math>: steroid versus control)</li> <li>• 1 month: 31.9 versus 37.2 versus 20.5 (ns)</li> <li>• 3 months: 31.2 versus 32.5 versus 31.0 (ns)</li> <li>• 6 months: 31.2 versus 37.1 versus 20.5 (ns)</li> </ul> </li> <li>• <b>NHP: Energy score (median percent</b></li> </ul>	
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				<p><b>change)</b></p> <ul style="list-style-type: none"> <li>• Baseline: 100 versus 88.0 versus 63.2 (ns)</li> <li>• 2 weeks: 60.8 versus 30.4 versus 63.2 (ns)</li> <li>• 1 month: 100 versus 24.0 versus 60.8 (ns)</li> <li>• 3 months: 62.0 versus 30.4 versus 100 (ns)</li> <li>• 6 months: 81.6 versus 48.8 versus 63.2 (ns)</li> </ul> <p>• <b>NHP: Sleep score (median percent change)</b></p> <ul style="list-style-type: none"> <li>• Baseline: 58.0 versus 55.9 versus 55.9 (ns)</li> <li>• 2 weeks: 26.2 versus 31.8 versus 12.5 (ns)</li> <li>• 1 month: 44.7 versus 12.5 versus 12.5 (ns)</li> <li>• 3 months: 14.3 versus 12.5 versus 28.6 (ns)</li> <li>• 6 months: 25.5 versus 12.5 versus 28.6 (ns)</li> </ul> <p>• <b>NHP: Social isolation score (median percent change)</b></p> <ul style="list-style-type: none"> <li>• Baseline: 41.7 versus 28.9 versus 0 (ns)</li> <li>• 2 weeks: 22.0 versus 18.0 versus 0 (ns)</li> <li>• 1 month: 22.0 versus 18.9 versus 0 (ns)</li> <li>• 3 months: 32.0 versus 11.0 versus 0 (ns)</li> <li>• 6 months: 32.3 versus 0 versus 0 (ns)</li> </ul> <p>• <b>NHP: Emotional reactions score (median percent change)</b></p> <ul style="list-style-type: none"> <li>• Baseline: 45.0 versus 33.0 versus</li> </ul>		
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				<p>23.7 (ns)</p> <ul style="list-style-type: none"> <li>• 2 weeks: 13.3 versus 17.1 versus 0 (ns)</li> <li>• 1 month: 46.1 versus 15.1 versus 9.7 (ns)</li> <li>• 3 months: 41.4 versus 0 versus 9.7 (ns)</li> <li>• 6 months: 27.5 versus 6.9 versus 0 (ns)</li> </ul> <p><b><u>Physical Activity</u></b></p> <ul style="list-style-type: none"> <li>• <b>Finger Floor Distance (cm) (mean)</b> <ul style="list-style-type: none"> <li>• Baseline: 9 versus 8 versus 6 (ns)</li> <li>• 2 weeks: 4 versus 9 versus 5 (ns)</li> <li>• 1 month: 5 versus 8 versus 3 (ns)</li> <li>• 3 months: 2 versus 6 versus 3 (ns)</li> <li>• 6 months: 2 versus 9 versus 4 (ns)</li> </ul> </li> <li>• <b>Treadmill Walk Test: time to first symptoms (sec) (mean)</b> <ul style="list-style-type: none"> <li>• Baseline: 100 versus 200 versus 90 (ns)</li> <li>• 2 weeks: 250 versus 280 versus 230 (ns)</li> <li>• 1 month: 260 versus 270 versus 270 (ns)</li> <li>• 3 months: 310 versus 380 versus 290 (ns)</li> <li>• 6 months: 250 versus 310 versus 380 (ns)</li> </ul> </li> <li>• <b>Treadmill Walk Test: total ambulation time (sec) (mean)</b> <ul style="list-style-type: none"> <li>• Baseline: 350 versus 450 versus 350 (ns)</li> <li>• 2 weeks: 480 versus 490 versus 470 (ns)</li> <li>• 1 month: 490 versus 460 versus 490 (ns)</li> <li>• 3 months: 570 versus 510 versus 570 (ns)</li> </ul> </li> </ul>		
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				<ul style="list-style-type: none"> <li>• 6 months: 540 versus 350 versus 620 (ns)</li> <li>• <b>Sit-to-Stand Test (sec) (mean)</b> <ul style="list-style-type: none"> <li>• Baseline: 2.1 versus 2.4 versus 2.2 (ns)</li> <li>• 2 weeks: 1.6 versus 2.1 versus 2.0 (ns)</li> <li>• 1 month: 1.6 versus 1.6 versus 2.0 (ns)</li> <li>• 3 months: 1.6 versus 1.3 versus 2.2 (ns)</li> <li>• 6 months: 1.7 versus 1.7 versus 2.0 (ns)</li> </ul> </li> <li>• <b>Weight-carrying test (sec) (mean)</b> <ul style="list-style-type: none"> <li>• Baseline: 19 versus 21 versus 19 (ns)</li> <li>• 2 weeks: 17 versus 18 versus 18 (ns)</li> <li>• 1 month: 18 versus 17 versus 17 (ns)</li> <li>• 3 months: 17 versus 16 versus 16 (ns)</li> <li>• 6 months: 18 versus 16 versus 17 (ns)</li> </ul> </li> </ul>		
<b>Ghahreman (2010)<sup>64</sup></b>	<b>RCT</b>  N = 150  Lumbar radicular pain  Acute (n = 80) or chronic (n = 70): <u>Acute</u> : median duration of symptoms (range for treatment groups): 3–8 weeks <u>Chronic</u> : median duration of	1 month (100% f/u, 150/150) (primary f/u)  *** <b>Once pts registered as having failed the treatment (pain relief &lt; 50% and registered their</b>	Transforaminal epidural (fluoroscopy guidance)  <u>Steroids used</u> : Triamcinolone (70 mg)  <u>Repeat injections</u> : at discretion of patient up to 3 injections (mean of 1.1 injections/pt as calculated by RH;	(1) <b>Transforaminal epidural steroid/local anesthetic (n = 28) versus</b> (2) <b>Transforaminal epidural local anesthetic (n = 27) versus</b> (3) <b>Transforaminal epidural saline (n = 37) versus</b> (4) <b>Intramuscular injection of steroids (n = 28) versus</b> (5) <b>Intramuscular injection of saline (n = 30)</b>  <b>Data reported for 1 month f/u:</b> <u>Pain</u> <ul style="list-style-type: none"> <li>• <b>Success (pain relief ≥ 50% &amp; did not register as (95% CI) (primary outcome)</b> </li> </ul>	NR	I Ib

	<p>symptoms (range for treatment groups): 32–96 weeks</p> <p>Median age: 43–49 years (range for each treatment group)</p> <p>59.3% male</p>	<p><b>failure), they were no longer followed.</b></p> <p>Patients were followed as long as they had a successful outcome.</p> <p>3-12 months (<math>\leq 23\%</math> f/u (34/150))</p>	<p>no patient required more than 2 injections)</p> <p><u>Cointerventions:</u> not restricted; all cointerventions reported</p>	<ul style="list-style-type: none"> <li>1 month: <ul style="list-style-type: none"> <li>(1) 54% (15/28) (95% CI, 36%, 72%) (statistically meaningful difference compared to any of the control tx groups (2-5)) (<math>P = \text{NR}</math>)</li> <li>(2) 7% (2/27) (95% CI, 0%, 17%)</li> <li>(3) 19% (7/37) (95% CI, 6%, 32%)</li> <li>(4) 21% (6/28) (95% CI, 6%, 36%)</li> <li>(5) 13% (4/30) (95% CI, 1%, 25%)</li> </ul> </li> <li>Median length of pain relief <math>\geq 50\%</math> <i>only for pts who had pain relief at one month:</i> <ul style="list-style-type: none"> <li>(1) 6 months (IQR: 1, 12) (<math>n = 15</math>) (ns)</li> <li>(2) 7 months (IQR: 1, 12) (<math>n = 2</math>)</li> <li>(3) 6 months (IQR: 3, 12) (<math>n = 7</math>)</li> <li>(4) 12 months (IQR: 11, 12) (<math>n = 6</math>)</li> <li>(5) 12 months (IQR: 8, 12) (<math>n = 4</math>)</li> </ul> </li> <li>Leg pain scores (VAS, 0 to 10 cm) (mean <math>\pm</math> SD): <ul style="list-style-type: none"> <li>Baseline: <ul style="list-style-type: none"> <li>(1) <math>7.0 \pm 1.7</math></li> <li>(2) <math>7.4 \pm 2.1</math></li> <li>(3) <math>6.6 \pm 2.2</math></li> <li>(4) <math>7.6 \pm 2.0</math></li> <li>(5) <math>7.0 \pm 1.5</math></li> </ul> </li> <li>1 month: <ul style="list-style-type: none"> <li>(1) <math>4.1 \pm 3.0</math> (<math>P \leq .05</math> for all comparitors except (3) (transforaminal saline)</li> <li>(2) <math>6.7 \pm 2.8</math></li> <li>(3) <math>5.5 \pm 2.6</math></li> <li>(4) <math>5.9 \pm 3.4</math></li> <li>(5) <math>6.0 \pm 2.5</math></li> </ul> </li> <li>Median length of pain relief <math>\geq 50\%</math> <i>only for pts who had pain relief at one month:</i></li> </ul> </li></ul>		
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				<p>(1) 6 months (IQR: 1, 12) (n = 15) (ns)</p> <p>(2) 7 months (IQR: 1, 12) (n = 2)</p> <p>(3) 6 months (IQR: 3, 12) (n = 7)</p> <p>(4) 12 months (IQR: 11, 12) (n = 6)</p> <p>(5) 12 months (IQR: 8, 12) (n = 4)</p> <p><b><u>One month outcomes for the “successful” versus “unsuccessful” patients in each treatment group</u></b></p> <p><b>NOTE:</b> baseline scores for successful versus unsuccessful were <u>not</u> statistically different in any group for any outcome reported below.</p> <p><b>Patient numbers:</b></p> <p>(1) (n = 15) versus (n = 13)</p> <p>(2) (n = 2) versus (n = 25)</p> <p>(3) (n = 7) versus (n = 30)</p> <p>(4) (n = 6) versus (n = 22)</p> <p>(5) (n = 4) versus (n = 26)</p> <p>• <b>Leg pain scores (VAS, 0 to 10 cm) (median (interquartile range)):</b></p> <p>(1) 2 (1–2) (n = 15) versus 7 (7–8) (<math>P = .000</math>)</p> <p>(2) 0 versus 8 (6–9) (<math>P</math> not calculable)</p> <p>(3) 1 (0–3) versus 7 (5–8) (<math>P = .001</math>)</p> <p>(4) 1 (0–2) versus 8 (6–10) (<math>P = .000</math>)</p> <p>(5) 1 (0–3) versus 7 (5–8) (<math>P = .002</math>)</p> <p>• <b>Roland-Morris scores (0–24) (median (interquartile range)):</b></p> <p>(1) 4 (0–9) versus 14 (10–23) (<math>P = .001</math>)</p> <p>(2) 8 (2–14) versus 18 (14–21) (ns)</p>		
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				<p>(3) 6 (2–7) versus 19 (16–20) (<math>P = .000</math>)</p> <p>(4) 5 (0–11) versus 16 (14–20) (<math>P = .012</math>)</p> <p>(5) 5 (0–12) versus 15 (11–19) (<math>P = .026</math>)</p> <p>• <b>SF-36 physical functioning (1–100) (median (interquartile range)):</b></p> <p>(1) 55 (40–65) versus 15 (5–42) (<math>P = .012</math>)</p> <p>(2) 63 (60–65) versus 35 (15–45) (ns)</p> <p>(3) 65 (45–70) versus 20 (10–35) (<math>P = .001</math>)</p> <p>(4) 60 (38–93) versus 30 (14–46) (<math>P = .014</math>)</p> <p>(5) 85 (66–89) versus 30 (19–53) (<math>P = .004</math>)</p> <p>• <b>SF-36 social functioning (1–100) (median (interquartile range)):</b></p> <p>(1) 88 (50–100) versus 38 (13–57) (<math>P = .001</math>)</p> <p>(2) 95 (88–100) versus 25 (19–57) (ns)</p> <p>(3) 88 (75–100) versus 38 (25–50) (<math>P = .001</math>)</p> <p>(4) 75 (56–100) versus 38 (25–63) (<math>P = .013</math>)</p> <p>(5) 88 (75–100) versus 50 (25–63) (<math>P = .010</math>)</p> <p>• <b>SF-36 bodily pain (1–100) (median (interquartile range)):</b></p> <p>(1) 62 (52–74) versus 21 (0–27) (<math>P = .000</math>)</p> <p>(2) 63 (41–84) versus 22 (10–31) (<math>P = .047</math>)</p> <p>(3) 61 (31–74) versus 22 (12–32) (<math>P = .001</math>)</p> <p>(4) 74 (50–88) versus 22 (21–34) (<math>P = .000</math>)</p>		
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				<p>= .001) (5) 73 (65–74) versus 22 (12–41) (<math>P</math> = .002)</p> <p>• <b>SF-36 general health (1–100) (median (interquartile range)):</b> (1) 62 (50–82) versus 60 (40–71) (ns) (2) 75 (72–77) versus 65 (41–79) (ns) (3) 82 (72–90) versus 61 (40–72) (<math>P</math> = .002) (4) 71 (44–82) versus 50 (35–76) (ns) (5) 75 (64–88) versus 64 (48–83) (ns)</p> <p>• <b>SF-36 mental health (1–100) (median (interquartile range)):</b> (1) 84 (68–96) versus 40 (28–68) (<math>P</math> = .001) (2) 72 (48–96) versus 52 (38–80) (ns) (3) 84 (68–100) versus 48 (35–68) (<math>P</math> = .003) (4) 66 (56–79) versus 60 (48–77) (ns) (5) 90 (85–95) versus 56 (36–77) (<math>P</math> = .007)</p> <p><b>Data reported for <math>\geq 12</math> months f/u</b> <b><u>Surgery</u></b> Surgery <math>\leq 12</math> months (as rescue treatment or after having registered treatment failure) (% patients): (1) 36% (10/28) (2) 26% (7/27) (3) 27% (10/37) (4) 21% (6/28) (5) 30% (9/30)</p>		
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				<p><b>Data reported for <math>\geq 12</math> months f/u only for pts who had pain relief at one month</b> <b><u>Pain</u></b></p> <ul style="list-style-type: none"> <li>Median length of pain relief <math>\geq 50\%</math> only for pts who had pain relief at one month: <ul style="list-style-type: none"> <li>(1) 6 months (IQR: 1, 12) (n = 15) (ns)</li> <li>(2) 7 months (IQR: 1, 12) (n = 2)</li> <li>(3) 6 months (IQR: 3, 12) (n = 7)</li> <li>(4) 12 months (IQR: 11, 12) (n = 6)</li> <li>(5) 12 months (IQR: 8, 12) (n = 4)</li> </ul> </li> </ul>		
<b>Tafazal (2009)<sup>197</sup></b>	<p><b>RCT</b></p> <p>N = 150</p> <p>LBP with disc herniation or foraminal stenosis</p> <p>Chronic (mean duration of symptoms: 18.9 months, interquartile range: 6 – 24.5 months)</p> <p>Mean age: 51.9 years</p> <p>35% female</p>	<p>6 weeks: 94% (141/150)</p> <p>3 months: 83% (124/150) ***</p> <p>12 months (median 20 months, range 12 – 31) 86% (129/150)</p>	<p>Transforaminal (peri-radicular) epidural (fluoroscopy guidance)</p> <p><u>Steroids used:</u> Methylprednisolone (depomedrone) (40 mg)</p> <p><u>Repeat injections:</u> (none) as needed with based on significant residual leg pain after at least 12 months (mean injections/year NR)</p> <p><u>Cointerventions:</u> patients agreed not to alter oral</p>	<p><b>Transforaminal epidural steroid/local anesthetic (n = 122) versus local anesthetic injection (n = 124) (mean scores)</b></p> <p><b><u>Pain</u></b></p> <ul style="list-style-type: none"> <li><b>Pain scores, leg pain (VAS, 0 to 100 mm):</b> <ul style="list-style-type: none"> <li>Baseline: 72.7 (60 – 80) versus 76.4 (70 – 90) (ns) (mean, interquartile range)</li> <li>6 weeks: <math>26.1 \pm 3.3</math> versus <math>18.6 \pm 3.4</math> (ns) (mean change from baseline <math>\pm</math> SE)</li> <li>12 weeks: <math>24.5 \pm 3.6</math> versus <math>22.6 \pm 4.1</math> (ns) (mean change from baseline <math>\pm</math> SE)</li> </ul> </li> <li><b>Pain scores, back pain (VAS, 0 to 100 mm) (mean, interquartile range):</b> <ul style="list-style-type: none"> <li>Baseline: 44.3 (20 – 73) versus 47.5 (20 – 80) (ns)</li> <li>6 weeks: <math>9.8 \pm 3.8</math> versus <math>6.4 \pm 3.6</math> (ns) (mean change from baseline <math>\pm</math></li> </ul> </li> </ul>	NR	I Ib

			analgesic medication and had no additional treatments, such as physical therapy, during study periods	<p>SE)</p> <ul style="list-style-type: none"> <li>12 weeks: <math>6.9 \pm 3.7</math> versus <math>9.9 \pm 3.8</math> (ns) (mean change from baseline <math>\pm</math> SE)</li> </ul> <p><b>Function</b></p> <ul style="list-style-type: none"> <li><b>ODI (0-100 scale):</b> <ul style="list-style-type: none"> <li>Baseline: 43.4 (32 – 54) versus 46.6 (34 – 58) (ns) (mean, interquartile range)</li> <li>6 weeks: <math>8.8 \pm 2.1</math> versus <math>8.5 \pm 2.1</math> (ns) (mean change from baseline <math>\pm</math> SE)</li> <li>12 weeks: <math>9.3 \pm 2.3</math> versus <math>10.7 \pm 2.6</math> (ns) (mean change from baseline <math>\pm</math> SE)</li> </ul> </li> <li><b>LBOS (0-75 scale):</b> <ul style="list-style-type: none"> <li>Baseline: 25.8 (17 – 34) versus 25 (16 – 32) (ns) (mean, interquartile range)</li> <li>6 weeks: <math>4.4 \pm 1.7</math> versus <math>5.4 \pm 1.8</math> (ns) (mean change from baseline <math>\pm</math> SE)</li> <li>12 weeks: <math>9.1 \pm 2.0</math> versus <math>9.4 \pm 2.3</math> (ns) (mean change from baseline <math>\pm</math> SE)</li> </ul> </li> </ul> <p><b>Additional interventions</b> †††</p> <ul style="list-style-type: none"> <li><b>Surgery (undefined) (% patients):</b> <ul style="list-style-type: none"> <li>12 months: 14.1% (9/64) versus 21.5% (14/65) (ns)</li> </ul> </li> <li><b>Transforaminal (peri-radicular) injections (% patients):</b> <ul style="list-style-type: none"> <li>12 months: 12.5% (8/64) versus 15.4% (10/65) (ns)</li> </ul> </li> </ul>		
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CMM: conservative medical management

f/u: follow-up

LBP: low back pain

LoE: level of evidence

NRS: Numerical Rating Scale

ns: not statistically significant

NR: not reported

ODI: Oswestry Disability Index

SD: standard deviation

SE: standard error

SLR: Straight Leg Rising test

VAS: Visual Analog Scale

RMDI: Roland Morris Disability Index

NHP: Nottingham Health Profile

LBOS: Low Back Outcome Score

- \* Data represents only patients with complete follow-up [Manchikanti, 2008 pt 1, 2, 3, and 4; Manchikanti, 2010, Evaluation of the effectiveness; Manchikanti (2010) Preliminary Results of a Randomized, Double-blind; Manchikanti, 2009, Preliminary Results of a Comparative; Manchikanti, 2009, A Comparative Effectiveness Evaluation; Koc, 2009]. Author does not indicate whether baseline data includes all patients, including those without complete follow-up [Murata, 2009].
- † Data carried forward: if a patient is lost to follow-up or unblinded (and hence withdrawn), Manchikanti's studies carries that patient's last available data forward to all subsequent data points. Thus, it appears that each follow-up has data for all patients available but often some of the data has actually been carried forward from the last available data point. Data from any follow-up in which < 20% of the data in either group was carried forward will not be included in our analysis.
- ‡ Employment status was determined at the time of enrollment. Employable category includes patients who were unemployed due to pain or were employed but on sick leave or laid off [Manchikanti, 2008 pt 1, 2, 3, and 4; Manchikanti, 2010, Evaluation of the effectiveness; Manchikanti (2010) Preliminary Results of a Randomized, Double-blind; Manchikanti, 2009, Preliminary Results of a Comparative; Manchikanti, 2009, A Comparative Effectiveness Evaluation]
- § Error in reporting the number of females in Group 1 in Table 1: article reports a total of 42 males and females with a total sample size of 35 [Manchikanti, 2010, Evaluation of the effectiveness...].
- \*\* Does not include 32 patients who underwent surgery after 2<sup>nd</sup> procedure [Sayegh, 2009].
- †† Treatment procedure:
  - Treatment group: targeted adhesiolysis, lidocaine + 10% saline + steroid + normal saline [Manchikanti, 2009, Preliminary Results of a Comparative; Manchikanti, 2009, A Comparative Effectiveness Evaluation]. Lidocaine + steroid in L2 [Murata, 2009].
  - Control group: non-targeted catheter up to S3, lidocaine + normal saline + steroid + normal saline [Manchikanti, 2009, Preliminary Results of a Comparative].
  - Control group: non-targeted catheter up to S3, lidocaine + 0.9% saline + steroid + normal saline (note: this is the procedure reported in the narration, which differs from Table 1 (control group reported to receive "normal saline" rather than 0.9% saline) [Manchikanti, 2009, A Comparative Effectiveness Evaluation].
  - Control group: lidocaine + steroid in back muscle in same area as L2 [Murata, 2009].
- ‡‡ Physical therapy group: passive methods for 2 weeks; Control group: no description provided. All outcome measure estimated from graph except NHP scores. All percent change differences between groups  $P = ns$  except as noted (RMDI and NHP subgroup scores). Finger floor distance: distance (cm) between finger tip and floor measured while patient is bent forward attempting to touch the floor. Treadmill walk test, total ambulation time (secs): patient walks until unable to walk due to severe pain, maximum of 15 minutes. Sit-to-stand test (secs): time for patient to rise from seated to standing position without using arms. Weight-carrying test (secs): time for patient to walk 20 m carrying 10% of body weight in hand-held weights [Koc, 2009].

§§ Author does not define “adequate therapeutic effect” or what assessment tool was used to measure pain [Murata, 2009].

\*\*\*Inconsistency in reporting follow-up. The author reported that 141 patients were available at the 6 week follow-up and 16 patients who did not attend 3 month follow-up, giving a total of 124 patients at the follow-up. Either 17 patients did not attend the 3 month follow-up or the number of patients at 3 month-follow-up should total 125 [Tafazal, 2009].

†††Additional undefined surgery or transforaminal (peri-radicular) injections given based on significant residual leg pain. Does not include one patient who received additional injection after 6 week followup and was omitted from the analysis thereafter [Tafazal, 2009].

### Appendix M. Efficacy data from RCTs: lumbar facet joint interventions

Author (Year)	Study type  No. patients randomized (N) Diagnosis Duration of symptoms Mean age (range) Sex	Duration of f/u (% complete f/u rate)	Injection approach (guidance) Steroids used Diagnostic block Repeat injections (mean no. of injections) Cointerventions	Main results	Conflict of interest	LoE
<b>Manchikanti (2010)</b> <sup>135*</sup> Evaluation of Lumbar Facet	<b>RCT</b>  N = 120  LBP of facet joint origin  Chronic ( $\geq 6$ months)  Mean age ( $\pm$ SD): 47 $\pm$ 16 <sup>†</sup> years  60% female <sup>†</sup>	3 months: 98% (118/120)  6 months: 92% (110/120)  12 months: 83% (99/120)  18 months: 73% (88/120)  24 months: 80% (96/120)  % patients	Facet joint nerve block (fluoroscopy guidance)  <u>Steroids used:</u> Betamethasone (0.075 – 0.225 mg)  <u>Repeat injections:</u> as needed with increasing pain (mean: 5 – 6 injections/24 months)  <u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)	<b>Facet joint nerve block steroid/local anesthetic versus local anesthetic injection (mean scores) <sup>†</sup></b>  (n = 42 per group, see info on % pts with data carried forward at each f/u)  <b><u>Pain</u></b> • <b>Pain scores (NRS, 0 to 10 cm) (mean <math>\pm</math> SD):</b> • Baseline: 7.9 $\pm$ 1.0 versus 8.2 $\pm$ 0.8 (ns) • 3 months: 3.5 $\pm$ 1.1 versus 3.8 $\pm$ 1.3 (ns) • 6 months: 3.3 $\pm$ 0.8 versus 3.6 $\pm$ 1.5 (ns) • 12 months: 3.5 $\pm$ 1.1 versus 3.7 $\pm$ 1.7 (ns) • <del>18 months: 3.3 <math>\pm</math> 1.0 versus 3.5 <math>\pm</math> 1.5 (ns)</del> • <del>24 months: 3.2 <math>\pm</math> 0.9 versus 3.5 <math>\pm</math> 1.5 (ns)</del> • <b>Pain relief, <math>\geq 50\%</math> (% patients):</b> • 3 months: 82% versus 83% (ns) • 6 months: 93% versus 83% (ns) • 12 months: 85% versus 82% (ns)	None	IIb

		<p>with data carried forward<sup>‡</sup> (steroid vs control):</p> <p>3 months: 0% (0/60) vs 3% (2/60)</p> <p>6 months: 5% (3/60) vs 12% (7/60)</p> <p>12 months: 20% (12/60) vs 15% (9/60)</p> <p>18 months: 28% (17/60) vs 20% (15/60)</p> <p>24 months: 20% (12/60) vs 20% (12/60)</p>		<ul style="list-style-type: none"> <li>• <del>18 months: 90% versus 85% (ns)</del> <sup>‡</sup></li> <li>• 24 months: 90% versus 85% (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>Function</u></b></p> <ul style="list-style-type: none"> <li>• <b>ODI (0-50 scale) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 25.9 <math>\pm</math> 5.0 versus 26.6 <math>\pm</math> 4.6 (<math>P = \text{NR}</math>)</li> <li>• 3 months: 13.5 <math>\pm</math> 5.6 versus 12.7 <math>\pm</math> 4.7 (<math>P = \text{NR}</math>)</li> <li>• 6 months: 12.2 <math>\pm</math> 5.0 versus 12.7 <math>\pm</math> 4.7 (<math>P = \text{NR}</math>)</li> <li>• 12 months: 12.0 <math>\pm</math> 5.4 versus 12.3 <math>\pm</math> 4.8 (<math>P = \text{NR}</math>)</li> <li>• <del>18 months: 11.2 <math>\pm</math> 4.9 versus 12.1 <math>\pm</math> 5.0 (<math>P = \text{NR}</math>)</del> <sup>‡</sup></li> <li>• 24 months: 11.0 <math>\pm</math> 4.8 versus 12.0 <math>\pm</math> 4.9 (<math>P = \text{NR}</math>)</li> </ul> </li> <li>• <b>Functional improvement, <math>\geq 40\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 72% versus 82% (<math>P = \text{NR}</math>)</li> <li>• 6 months: 78% versus 83% (<math>P = \text{NR}</math>)</li> <li>• 12 months: 78% versus 85% (<math>P = \text{NR}</math>)</li> <li>• <del>18 months: 87% versus 83% (<math>P = \text{NR}</math>)</del> <sup>‡</sup></li> <li>• 24 months: 88% versus 87% (<math>P = \text{NR}</math>)</li> </ul> </li> </ul> <p><b><u>Opioid intake (morphine equivalents in mg/day)</u></b></p> <ul style="list-style-type: none"> <li>• Baseline: 37 <math>\pm</math> 40.4 versus 31 <math>\pm</math> 25.2 (ns)</li> <li>• 12 months: 33 <math>\pm</math> 31.1 versus 29 <math>\pm</math> 25.6 (ns)</li> <li>• 24 months: 30 <math>\pm</math> 27.1 versus 27 <math>\pm</math> 23.8 (ns)</li> </ul> <p><b><u>Employed (part-time or full-time) (% of patients eligible for employment)</u></b> <sup>§</sup></p> <ul style="list-style-type: none"> <li>• Baseline: 74% (17/23) versus 56% (10/18) (<math>P = \text{NR}</math>)</li> <li>• 12 months: 88% (22/25) versus 94% (16/17) (<math>P = \text{NR}</math>)<sup>†</sup></li> <li>• 24 months: 92% (22/24) versus 89% (16/18) (<math>P = \text{NR}</math>)</li> </ul>	
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				<p><b><u>Total relief with sequential procedures (weeks) (mean)</u></b></p> <ul style="list-style-type: none"> <li>• Overall total relief: (n = 60) <math>84 \pm 27.5</math> versus (n = 60) <math>82 \pm 31.8</math> (<math>P = \text{NR}</math>)</li> <li>• Injection #1: (n = 4) <math>59 \pm 51.7</math> versus (n = 7) <math>42 \pm 47.1</math> (<math>P = \text{NR}</math>)</li> <li>• after 2<sup>nd</sup> injection: (n = 6) <math>58 \pm 42.6</math> versus (n = 4) <math>79 \pm 51.0</math> (<math>P = \text{NR}</math>)</li> <li>• after 3<sup>rd</sup> injection: (n = 4) <math>63 \pm 32.6</math> versus (n = 8) <math>63 \pm 37.8</math> (<math>P = \text{NR}</math>)</li> <li>• after 4<sup>th</sup> injection: (n = 8) <math>71 \pm 27.7</math> versus (n = 2) <math>71 \pm 47.4</math> (<math>P = \text{NR}</math>)</li> <li>• after 5<sup>th</sup> injection: (n = 5) <math>89 \pm 14.4</math> versus (n = 3) <math>81 \pm 28.5</math> (<math>P = \text{NR}</math>)</li> <li>• after 6<sup>th</sup> injection: (n = 5) <math>88 \pm 17.6</math> versus (n = 5) <math>80 \pm 20.3</math> (<math>P = \text{NR}</math>)</li> <li>• after 7<sup>th</sup> injection: (n = 6) <math>91 \pm 14.5</math> versus (n = 10) <math>93 \pm 4.8</math> (<math>P = \text{NR}</math>)</li> <li>• after 8<sup>th</sup> injection: (n = 20) <math>99 \pm 4.8</math> versus (n = 18) <math>100 \pm 5.1</math> (<math>P = \text{NR}</math>)</li> <li>• after 9<sup>th</sup> injection: (n = 2) <math>103 \pm 0.7</math> versus (n = 3) <math>99 \pm 3.8</math> (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>Average relief per procedure (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• Overall relief per procedure: (n = 60) <math>19 \pm 18.2</math> versus (n = 60) <math>19 \pm 19.9</math> (<math>P = \text{NR}</math>)</li> <li>• Injection #1: (n = 4) <math>59 \pm 51.7</math> versus (n = 7) <math>42 \pm 47.1</math> (<math>P = \text{NR}</math>)</li> <li>• after 2<sup>nd</sup> injection: (n = 6) <math>29 \pm 21.3</math> versus (n = 4) <math>39 \pm 25.5</math> (<math>P = \text{NR}</math>)</li> <li>• after 3<sup>rd</sup> injection: (n = 4) <math>21 \pm 10.9</math> versus (n = 8) <math>21 \pm 12.6</math> (<math>P = \text{NR}</math>)</li> <li>• after 4<sup>th</sup> injection: (n = 8) <math>18 \pm 6.9</math> versus (n = 2) <math>18 \pm 11.8</math> (<math>P = \text{NR}</math>)</li> <li>• after 5<sup>th</sup> injection: (n = 5) <math>18 \pm 2.9</math> versus (n = 3) <math>16 \pm 5.8</math> (<math>P = \text{NR}</math>)</li> <li>• after 6<sup>th</sup> injection: (n = 5) <math>15 \pm 2.9</math> versus (n = 5) <math>13 \pm 3.8</math> (<math>P = \text{NR}</math>)</li> </ul>		
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				<ul style="list-style-type: none"> <li>• after 7<sup>th</sup> injection: (n = 6) 13 ± 2.1 versus (n = 10) 13 ± 0.7 (<i>P</i> = NR)</li> <li>• after 8<sup>th</sup> injection: (n = 20) 12 ± 0.6 versus (n = 18) 13 ± 0.6 (<i>P</i> = NR)</li> <li>• after 9<sup>th</sup> injection: (n = 2) 11 ± 0.1 versus (n = 3) 11 ± 0.4 (<i>P</i> = NR)</li> </ul>		
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CMM: conservative medical management

f/u: follow-up

LBP: low back pain

LoE: level of evidence

NRS: Numerical Rating Scale

ns: not statistically significant

NR: not reported

ODI: Oswestry Disability Index

SD: standard deviation

\*This report states that the original patient assignments were as follows: 30 patients within each treatment subgroup (steroid/anesthetic or steroid/anesthetic plus Sarapin) and 30 patients within each control group (anesthetic or anesthetic plus Sarapin) for a total sample size of 120 patients. No significant differences in any outcome measure were found between the Sarapin and non-Sarapin groups, so all results are reported for treatment (steroid + anesthetic) versus control (anesthetic only) [Manchikanti, 2010,Evaluation of Lumbar Facet].

† Data represents only patients with complete follow-up [Manchikanti, 2010,Evaluation of Lumbar Facet].

‡ Data carried forward: if a patient is lost to follow-up or unblinded (and hence withdrawn), Manchikanti's studies carries that patient's last available data forward to all subsequent data points. Thus, it appears that each follow-up has data for all patients available but often some of the data has actually been carried forward from the last available data point. Data from any follow-up in which < 20% of the data in either group was carried forward will not be included in our analysis.

§ Employment status was determined at the time of enrollment. Employable category includes patients unemployed or employed on a part-time basis with limited or no employment due to pain. For the 24 month follow-up, the total patients eligible for employment includes 1 patient over 65 years of age who returned to work in the treatment group [Manchikanti, 2010,Evaluation of Lumbar Facet].

**Appendix N. Efficacy data from RCTs: lumbar intradiscal injections**

Author (Year)	Study type  No. patients randomized (N) Diagnosis Duration of symptoms Mean age (range) Sex	Duration of f/u (% complete f/u rate)	Injection approach (guidance) Steroids used Diagnostic block Repeat injections (mean no. of injections) Cointerventions	Main results	Conflict of interest	LoE
<b>Peng (2010)</b> <sup>161</sup>	<b>RCT</b>  N = 72  LBP without radiculopathy and with lumbar disc degeneration  Chronic (mean duration 3.4 ±1.7 years)  Mean age (± SD): 42 ± 13.3 years  43% female	6, 12, 24 months(98.6% f/u; 71/72)	lumbar intradiscal(under fluoroscopy guidance)  <u>Steroids used</u> none Treatment: Methylene blue (10 mg)  <u>Repeat injections:</u> (mean injections/year NR)  <u>Cointerventions:</u> bedrest for 24 hours and patients asked to avoid strenuous exercise for 3 weeks	<b>Intradiscal Methylene blue/local anesthetic (n = 36) versus saline/local anesthetic (n = 36) (mean scores)</b>  <u>Pain</u> • <b>Pain scores (NRS, 0 to 100 cm) (mean ± SD):</b> • Baseline: 72.33 ± 12.35 versus 67.28 ± 11.45 (ns) • 6 months: 24.94 ± 17.38 versus 63.51 ± 11.66 ( <i>P</i> < .001) • 12 months: 21.58 ± 17.93 versus 62.40 ± 12.05 ( <i>P</i> < .001) • 24 months: 19.83 ± 16.03 versus 60.37 ± 14.10 ( <i>P</i> < .001) • <b>Pain relief*</b> • 6 months, complete relief: 19% (7/36) versus NR ( <i>P</i> = NR) • 6 months, dramatic improvement: 28% (10/36) versus NR ( <i>P</i> = NR) • 6 months, obvious improvement: 42% (15/36) versus NR ( <i>P</i> = NR)  <u>Function</u> • <b>ODI (0-100 scale) (mean ± SD):</b> • Baseline: 48.47 ± 5.12 versus 49.37 ± 6.79 (ns)	Although author stated no conflict of interest, work was supported by grant for scientific research from 304 <sup>th</sup> Hospital and the Foundation of Capital Medical Development, Beijing.	IIa

				<ul style="list-style-type: none"> <li>• 6 months: 16.00 ± 11.91 versus 48.40 ± 7.77 (<math>P &lt; .001</math>)</li> <li>• 12 months: 14.39 ± 12.87 versus 49.09 ± 10.20 (<math>P &lt; .001</math>)</li> <li>• 24 months: 12.89 ± 11.95 versus 47.69 ± 10.92 (<math>P &lt; .001</math>)</li> </ul> <p><b><u>Patient Satisfaction (% patients)<sup>†</sup></u></b></p> <ul style="list-style-type: none"> <li>• 24 months, completely satisfied: 19.4% (7/36) versus 0% (0/35) (<math>P &lt; .001</math>)</li> <li>• 24 months, satisfied: 72.2% (26/36) versus 14.3% (5/35) (<math>P &lt; .001</math>)</li> <li>• 24 months, unsatisfied: 8.4% (3/36) versus 85.7% (30/35) (<math>P &lt; .001</math>)</li> </ul> <p><b><u>Medication usage<sup>‡</sup></u></b></p> <ul style="list-style-type: none"> <li>• 24 months, none: 83.3% (30/36) versus 5.7% (2/35) (<math>P &lt; .001</math>)</li> <li>• 24 months, occasional: 8.3% (3/36) versus 51.4% (18/35) (<math>P &lt; .001</math>)</li> <li>• 24 months, regular: 8.3% (3/36) versus 42.9% (15/35) (<math>P &lt; .001</math>)</li> </ul>		
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f/u: follow-up

LBP: low back pain

LoE: level of evidence

NRS: Numerical Rating Scale

ns: not statistically significant

NR: not reported

ODI: Oswestry Disability Index

SD: standard deviation

\*Pain relief defined as: complete relief (NRS = 0 – 10); Dramatic improvement (NRS < 20 points); Obvious improvement (reduction in NRS score ≤ 20 points) [Peng, 2010].

<sup>†</sup>Patient satisfaction defined as: Completely satisfied = no back pain at all time and no restriction of activities; Satisfied = slight pain that requires no medication and mild restriction of activities; Unsatisfied = moderate to severe pain that requires medication and moderate to severe restriction of activities [Peng, 2010].

<sup>‡</sup>Medication usage includes nonsteroidal anti-inflammatory drugs or opioid medications; dosages not specified and categories not defined. Patients advised to avoid taking medication at least 24 hours before outcome assessment at all follow-ups [Peng, 2010].

**Appendix O. Efficacy data from RCTs: cervical epidural injections**

Author (Year)	Study type  No. patients randomized (N) Diagnosis Duration of symptoms Mean age (range) Sex	Duration of f/u (% complete f/u rate)	Injection approach (guidance) Steroids used Diagnostic block Repeat injections (mean no. of injections) Cointerventions	Main results	Conflict of interest	LoE
<b>Manchikanti (2010)</b> <sup>124</sup> Cervical Epidural Injections	<b>RCT</b>  N = 120  CNP without disc herniation or radiculitis  Chronic ( $\geq 6$ months)  Mean age ( $\pm$ SD): 44.5 $\pm$ 12.0* years  66% female*	3 months: 58% (70/120)  6 months: 57% (68/120)  12 months: 56% (67/120)  % patients with data carried forward† (steroid vs control):  3 months: 0% (0/35) vs 0% (0/35)  6 months: 3% (1/35) vs	Interlaminar epidural (fluoroscopy guidance); 27% between T1/C7; 64% between C6/ C7; 9% between C5/C6  <u>Steroids used:</u> Betamethasone (6 mg)  <u>Repeat injections:</u> as needed with increasing pain (mean: 3.9 $\pm$ 1.0 injections/year)  <u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)	<b>Interlaminar epidural steroid/local anesthetic versus local anesthetic injection (mean scores)</b>  (n = 35 per group, see info on % pts with data carried forward at each f/u)  <b><u>Pain</u></b> • <b>Pain scores (NRS, 0 to 10 cm)</b> (mean $\pm$ SD): • Baseline: 7.4 $\pm$ 0.9 versus 7.8 $\pm$ 0.8 (ns) • 3 months: 3.1 $\pm$ 1.0 versus 3.4 $\pm$ 1.4 (ns) • 6 months: 3.2 $\pm$ 1.0 versus 3.5 $\pm$ 1.5 (ns) • 12 months: 3.2 $\pm$ 1.1 versus 3.5 $\pm$ 1.3 (ns) • <b>Pain relief, <math>\geq 50\%</math> (% patients):</b> • 3 months: 86% versus 77% ( $P$ = NR) • 6 months: 86% versus 80% ( $P$ = NR) • 12 months: 80% versus 80% ( $P$ = NR) <b><u>Function</u></b> • <b>NDI (0-50 scale) (mean <math>\pm</math> SD):</b>	None	IIb

		<p>3% (1/35)</p> <p>12 months: 6% (2/35) vs 3% (1/35)</p>		<ul style="list-style-type: none"> <li>• Baseline: <math>28.5 \pm 7.0</math> versus <math>30.0 \pm 4.8</math> (ns)</li> <li>• 3 months: <math>13.1 \pm 4.9</math> versus <math>15.1 \pm 5.9</math> (ns)</li> <li>• 6 months: <math>13.1 \pm 5.2</math> versus <math>14.5 \pm 5.8</math> (ns)</li> <li>• 12 months: <math>12.7 \pm 4.9</math> versus <math>14.4 \pm 5.6</math> (ns)</li> <li>• <b>Functional improvement, <math>\geq 50\%</math> (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 80% versus 71% (ns)</li> <li>• 6 months: 83% versus 71% (ns)</li> <li>• 12 months: 80% versus 69% (ns)</li> </ul> </li> <li>• <b><u>Opioid intake (morphine equivalents in mg)</u></b> <ul style="list-style-type: none"> <li>• Baseline: <math>47.6 \pm 40.9</math> versus <math>60.7 \pm 59.8</math> (ns)</li> <li>• 3 months: <math>36.1 \pm 23.9</math> versus <math>51.1 \pm 53.7</math> (ns)</li> <li>• 6 months: <math>36.1 \pm 23.9</math> versus <math>50.5 \pm 53.7</math> (ns)</li> <li>• 12 months: <math>36.4 \pm 23.9</math> versus <math>50.5 \pm 53.7</math> (ns)</li> </ul> </li> <li>• <b><u>Employed (part-time or full-time) (% of patients eligible for employment)<sup>‡</sup></u></b> <ul style="list-style-type: none"> <li>• Baseline: 71% (10/14) versus 42% (5/12) (<math>P = \text{NR}</math>)</li> <li>• 12 months: 79% (11/14) versus 75% (9/12) (<math>P = \text{NR}</math>)</li> </ul> </li> <li>• <b><u>No. of injections/year</u></b> <ul style="list-style-type: none"> <li>• 12 months: <math>3.8 \pm 0.9</math> versus <math>3.9 \pm 1.1</math> (<math>P = \text{NR}</math>)</li> </ul> </li> <li>• <b><u>Total relief (weeks)</u></b> <ul style="list-style-type: none"> <li>• Injection #1: (n = 35) <math>8.0 \pm 7.9</math> versus (n = 35) <math>6.1 \pm 5.2</math> (<math>P = \text{NR}</math>)</li> <li>• after 2<sup>nd</sup> injection: (n = 34) <math>10.5 \pm 6.6</math> versus (n = 35) <math>10.2 \pm 6.2</math> (<math>P = \text{NR}</math>)</li> </ul> </li> </ul>		
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				<ul style="list-style-type: none"> <li>• after 3<sup>rd</sup> injection: (n = 32) 11.3 ± 4.1 versus (n = 31) 11.7 ± 6.7 (<i>P</i> = NR)</li> <li>• after 4<sup>th</sup> injection: (n = 27) 12.2 ± 2.6 versus (n = 23) 12.8 ± 2.8 (<i>P</i> = NR)</li> <li>• after 5<sup>th</sup> injection: (n = 6) 13.2 ± 0.4 versus (n = 11) 10.1 ± 5.2 (<i>P</i> = NR)</li> <li>• after 12 months (mean): 39.7 ± 13.6 versus 37.6 ± 16.2 (ns)</li> </ul> <p><b><u>Average relief per procedure (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• 10.6 ± 4.9 versus 9.7 ± 4.3 (<i>P</i> = NR)</li> </ul> <p><b><u>Average relief per procedure, 3<sup>rd</sup> procedure and after (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• (n = 29) 12.0 ± 4.0 versus (n = 29) 11.3 ± 4.9 (<i>P</i> = NR)</li> </ul>		
<b>Manchikanti (2010)<sup>125</sup></b> Effectiveness of Fluoroscopic	<b>RCT</b>  N = 120  CNP with disc herniation and radiculitis  Chronic (≥ 6 months)  Mean age (± SD): 46.1 ± 10.6* years  64% female*	3 months: 58% (70/120)  6 months: 57% (68/120)  12 months: 56% (67/120)  <hr/> % patients with data carried forward† (steroid vs control):  3 months:	Interlaminar epidural (fluoroscopy guidance); 31% between T1/C7; 60% between C6/C7; 9% between C5/C6  <u>Steroids used:</u> Betamethasone (6 mg)  <u>Repeat injections:</u> as needed with increasing pain (mean: 3.7 ± 1.2 injections/year)  <u>Cointerventions:</u> not required/	<b>Interlaminar epidural steroid/local anesthetic versus local anesthetic injection (mean scores)</b>  <b>(n = 35 per group, see info on % pts with data carried forward at each f/u)</b>  <u>Pain</u> <ul style="list-style-type: none"> <li>• <b>Pain scores (NRS, 0 to 10 cm) (mean ± SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 7.6 ± 0.9 versus 7.8 ± 0.9 (ns)</li> <li>• 3 months: 3.4 ± 1.1 versus 3.2 ± 1.1 (ns)</li> <li>• 6 months: 3.4 ± 1.0 versus 3.2 ± 1.1 (ns)</li> <li>• 12 months: 3.5 ± 1.2 versus 3.3 ± 1.2 (ns)</li> </ul> </li> <li>• <b>Pain relief, ≥ 50% (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 83% versus 89% (ns)</li> </ul> </li> </ul>	None	IIb

		<p>0% (0/35) vs 0% (0/35)</p> <p>6 months: 3% (1/35) vs 3% (1/35)</p> <p>12 months: 6% (2/35) vs 3% (1/35)</p>	<p>uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• 6 months: 74% versus 77% (ns)</li> <li>• 12 months: 77% versus 77% (ns)</li> </ul> <p><b><u>Function</u></b></p> <ul style="list-style-type: none"> <li>• <b>NDI (0-50 scale) (mean <math>\pm</math> SD):</b> <ul style="list-style-type: none"> <li>• Baseline: 28.7 <math>\pm</math> 8.4 versus 29.8 <math>\pm</math> 5.6 (ns)</li> <li>• 3 months: 14.1 <math>\pm</math> 5.6 versus 14.6 <math>\pm</math> 5.7 (ns)</li> <li>• 6 months: 13.9 <math>\pm</math> 5.7 versus 13.1 <math>\pm</math> 5.5 (ns)</li> <li>• 12 months: 13.8 <math>\pm</math> 5.5 versus 13.5 <math>\pm</math> 5.3 (ns)</li> </ul> </li> <li>• <b>Functional improvement, <math>\geq</math> 50% (% patients):</b> <ul style="list-style-type: none"> <li>• 3 months: 77% versus 77% (ns)</li> <li>• 6 months: 77% versus 86% (ns)</li> <li>• 12 months: 71% versus 74% (ns)</li> </ul> </li> </ul> <p><b><u>Opioid intake (morphine equivalents in mg)</u></b></p> <ul style="list-style-type: none"> <li>• Baseline: 54.5 <math>\pm</math> 63.2 versus 61.9 <math>\pm</math> 54.1 (ns)</li> <li>• 3 months: 42.8 <math>\pm</math> 43.9 versus 50.5 <math>\pm</math> 47.9 (ns)</li> <li>• 6 months: 42.1 <math>\pm</math> 44.4 versus 48.5 <math>\pm</math> 47.3 (ns)</li> <li>• 12 months: 41.6 <math>\pm</math> 44.9 versus 48.5 <math>\pm</math> 47.3 (ns)</li> </ul> <p><b><u>Employed (part-time or full-time) (% of patients eligible for employment)<sup>‡</sup></u></b></p> <ul style="list-style-type: none"> <li>• Baseline: 83% (10/12) versus 55% (6/11) (<math>P = \text{NR}</math>)</li> <li>• 12 months: 75% (9/12) versus 64% (7/11) (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>No. of injections/year</u></b></p> <ul style="list-style-type: none"> <li>• 12 months: 3.7 <math>\pm</math> 1.2 versus 3.7 <math>\pm</math> 1.1 (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>Total relief (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• Injection #1: (n = 35) 5.8 <math>\pm</math> 4.4</li> </ul>		
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				<p>versus (n = 35) <math>8.3 \pm 9.2</math> (<math>P = \text{NR}</math>)</p> <ul style="list-style-type: none"> <li>• after 2<sup>nd</sup> injection: (n = 32) <math>11.1 \pm 6.6</math> versus (n = 34) <math>10.3 \pm 5.4</math> (<math>P = \text{NR}</math>)</li> <li>• after 3<sup>rd</sup> injection: (n = 29) <math>12.5 \pm 5.4</math> versus (n = 23) <math>11.7 \pm 5.9</math> (<math>P = \text{NR}</math>)</li> <li>• after 4<sup>th</sup> injection: (n = 25) <math>11.6 \pm 2.4</math> versus (n = 23) <math>12.2 \pm 2.2</math> (<math>P = \text{NR}</math>)</li> <li>• after 5<sup>th</sup> injection: (n = 10) <math>11.6 \pm 2.5</math> versus (n = 8) <math>7.5 \pm 5.6</math> (<math>P = \text{NR}</math>)</li> <li>• after 12 months (mean): <math>37.7 \pm 15.4</math> versus <math>37.9 \pm 13.2</math> (ns)</li> </ul> <p><b><u>Average relief per procedure (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• <math>9.8 \pm 4.1</math> versus <math>11.3 \pm 8.3</math> (<math>P = \text{NR}</math>)</li> </ul>		
<p><b>Stav (1993)<sup>193</sup></b></p>	<p><b>RCT</b></p> <p>N = 50§</p> <p>CNP with resistant cervicobrachialgia</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): <math>51.1 \pm 2.7^*</math> years</p> <p>55% female*</p>	<p>1 week, 12 months: (84% f/u; 42/50)</p>	<p>Cervical epidural(no fluoroscopy guidance);into C5-C6 or C6-C7 interspace</p> <p><u>Steroids used:</u> Methylprednisolone sodium acetate (80 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain at 2 week intervals (mean: <math>2.5 \pm 0.16</math> injections)</p> <p><u>Cointerventions:</u> not required/</p>	<p><b>Cervical epidural steroid/local anesthetic (n = 25) versus posterior neck muscle steroid/local anesthetic injection (n = 17) (mean scores)</b></p> <p><b><u>Pain</u></b></p> <ul style="list-style-type: none"> <li>• <b>Pain relief** (based on VAS) (% patients):</b> <ul style="list-style-type: none"> <li>• 1 week, very good: 44% versus 17.6% (<math>P = .0377</math>)</li> <li>• 1 week, good: 32% versus 17.6% (<math>P = \text{NR}</math>)</li> <li>• 1 week, satisfactory: 8% versus 23.6% (<math>P = \text{NR}</math>)</li> <li>• 1 week, poor: 8% versus 29.4% (<math>P = \text{NR}</math>)</li> <li>• 1 week, worse: 8% versus 11.8% (<math>P = \text{NR}</math>)</li> <li>• 1 year, very good: 56% versus 5.9% (<math>P = .0004</math>)</li> </ul> </li> </ul>	NR	Iib

			uncontrolled (CMM by patient choice)	<ul style="list-style-type: none"> <li>• 1 year, good: 12% versus 5.9% (<math>P = \text{NR}</math>)</li> <li>• 1 year, satisfactory: 20% versus 17.6% (<math>P = \text{NR}</math>)</li> <li>• 1 year, poor: 4% versus 58.8% (<math>P = \text{NR}</math>)</li> <li>• 1 year, worse: 8% versus 11.8% (<math>P = \text{NR}</math>)</li> <li>• <b>Pain relief (based on VAS) (% patients), combined improvement groups:</b> <ul style="list-style-type: none"> <li>• 1 week, very good or good: 76% versus 35.2% (<math>P = .004</math>)</li> <li>• 1 year, very good or good: 68% versus 11.8% (<math>P = .0002</math>)</li> </ul> </li> </ul> <p><b><u>ROM<sup>††</sup></u></b></p> <ul style="list-style-type: none"> <li>• <b>ROM percent improvement:</b> <ul style="list-style-type: none"> <li>• 1 week: 82% versus 38% (<math>P = .033</math>)</li> <li>• 1 year: 69% versus 13% (<math>P = .024</math>)</li> </ul> </li> </ul> <p><b><u>Analgesic use, decrease in daily dose (% patients)</u></b></p> <ul style="list-style-type: none"> <li>• 1 week: 81.7% versus 8.6 (<math>P &lt; .05</math>)</li> <li>• 1 year: 63.9% versus 9.4% (<math>P &lt; .05</math>)</li> </ul> <p><b><u>Recovering the ability to work (% patients)</u></b></p> <ul style="list-style-type: none"> <li>• 1 week: 69.4% versus 12.8 (<math>P &lt; .05</math>)</li> <li>• 1 year: 61.3% versus 15.9% (<math>P &lt; .05</math>)</li> </ul>		
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CNP: cervical neck pain

CMM: conservative medical management

f/u: follow-up

LoE: level of evidence

NRS: Numerical Rating Scale

ns: not statistically significant

NR: not reported

NDI: Neck Disability Index

SD: standard deviation

ROM: range of motion

VAS: Visual Analog Scale

\* Data represents only patients with complete follow-up [Manchikanti, 2010, Cervical Epidural Injections; Manchikanti, 2010, Effectiveness of Fluoroscopic] or for most patients with follow-up ( $n = 40$ ) [Stav, 1993].

† Data carried forward: if a patient is lost to follow-up or unblinded (and hence withdrawn), Manchikanti's studies carries that patient's last available data forward to all subsequent data points. Thus, it appears that each follow-up has data for all patients available but often some of the data has actually been carried forward from the last available data point. Data from any follow-up in which  $< 20\%$  of the data in either group was carried forward will not be included in our analysis.

‡ Employment status was determined at the time of enrollment. Employable category includes patients unemployed or employed on a part-time basis with limited or no employment due to pain. [Manchikanti, 2010, Cervical Epidural Injections; Manchikanti, 2010, Effectiveness of Fluoroscopic]

§ Five patients in each group started placebo treatment (posterior intramuscular injection) during initial exam, then received treatment per randomization [Stav, 1993].

\*\* Pain relief was calculated by VAS as percent improvement: very good  $\geq 75\%$ ; good,  $50 - 74\%$ ; satisfactory,  $31 - 49\%$ ; poor  $\leq 30\%$ ; worse, increase in the intensity of pain [Stav, 1993].

†† ROM of the neck was defined as flexion, extension, and rotation to the left and right and was estimated from a graph [Stav, 1993].

**Appendix P. Efficacy data from RCTs: cervical facet joint interventions**

Author (Year)	Study type  No. patients randomized (N) Diagnosis Duration of symptoms Mean age (range) Sex	Duration of f/u (% complete f/u rate)	Injection approach (guidance) Steroids used Diagnostic block Repeat injections (mean no. of injections) Cointerventions	Main results	Conflict of interest	LoE
<b>Manchikanti (2008)<sup>137*</sup></b> Cervical Medial Branch Blocks <b>Manchikanti, 2006<sup>126</sup></b>	<b>RCT</b>  N = 120  CNP of facet joint origin  Chronic ( $\geq 6$ months)  Mean age ( $\pm$ SD): 44.5 $\pm$ 13.5 <sup>†</sup> years  74% female <sup>†</sup>	3 months: 98% (118/120)  6 months: 93% (111/120)  12 months: 88% (106/120)  % patients with data carried forward <sup>‡</sup> (steroid vs control):  3 months: 2% (1/60) vs 2% (1/60)  6 months: 8% (5/60) vs	medial branch block(fluoroscopy guidance)  <u>Steroids used:</u> Betamethasone (0.075 – 0.225 mg)  <u>Repeat injections:</u> as needed with increasing pain (mean: 3.5 $\pm$ 1.0 injections/year)  <u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)	<b>Medial branch block steroid/local anesthetic versus local anesthetic injection (mean scores)</b>  (n = 60 per group, see info on % pts with data carried forward at each f/u)  <u>Pain</u> <ul style="list-style-type: none"> <li>• Pain scores (NRS, 0 to 10 cm) (mean <math>\pm</math> SD): <ul style="list-style-type: none"> <li>• Baseline: 8.2 <math>\pm</math> 1.1 versus 8.2 <math>\pm</math> 0.8 (ns)</li> <li>• 3 months: 3.7 <math>\pm</math> 0.9 versus 3.8 <math>\pm</math> 1.0 (ns)</li> <li>• 6 months: 3.4 <math>\pm</math> 0.7 versus 3.6 <math>\pm</math> 1.1 (ns)</li> <li>• 12 months: 3.4 <math>\pm</math> 0.9 versus 3.7 <math>\pm</math> 1.2 (ns)</li> </ul> </li> <li>• Pain relief, <math>\geq 50\%</math> (% patients): § <ul style="list-style-type: none"> <li>• 3 months: 87% versus 84% (ns)</li> <li>• 6 months: 93% versus 87% (ns)</li> <li>• 12 months: 90% versus 90% (ns)</li> </ul> </li> </ul> <u>Function</u> <ul style="list-style-type: none"> <li>• NDI (0-50 scale) (mean <math>\pm</math> SD): <ul style="list-style-type: none"> <li>• Baseline: 25.1 <math>\pm</math> 5.0 versus 25.4 <math>\pm</math> 5.7 (ns)</li> <li>• 3 months: 12.2 <math>\pm</math> 4.6 versus 12.0 <math>\pm</math> 5.2 (ns)</li> <li>• 6 months: 11.6 <math>\pm</math> 4.2 versus 12.0 <math>\pm</math> 5.6 (ns)</li> <li>• 12 months: 11.7 <math>\pm</math> 4.6 versus 11.7 <math>\pm</math> 5.0</li> </ul> </li> </ul>	None	I Ib

		<p>7% (4/60)</p> <p>12 months: 10% (6/60) vs 13% (8/60)</p>		<p>(ns)</p> <ul style="list-style-type: none"> <li>• <b>Functional improvement (% patients):</b> <ul style="list-style-type: none"> <li>• <math>\geq 40\%</math>: 85% versus 85% (f/u period NR, <math>P = \text{NR}</math>)</li> <li>• <math>\geq 50\%</math>: 68% versus 63% (f/u period NR, <math>P = \text{NR}</math>)</li> </ul> </li> </ul> <p><b><u>Opioid intake (% patients)**</u></b></p> <ul style="list-style-type: none"> <li>• Baseline, no intake: 0% (0/30) versus 0% (0/30) (ns)</li> <li>• Baseline, mild intake: 13% (4/30) versus 13% (4/30) (ns)</li> <li>• Baseline, moderate intake: 64% (19/30) versus 70% (21/30) (ns)</li> <li>• Baseline, significant intake: 23% (7/30) versus 17% (5/30) (ns)</li> <li>• 12 months, no intake: 3% (1/30) versus 7% (2/30) (ns)</li> <li>• 12 months, mild intake: 0% (0/30) versus 3% (1/30) (ns)</li> <li>• 12 months, moderate intake: 70% (21/30) versus 70% (21/30) (ns)</li> <li>• 12 months, significant intake: 27% (8/30) versus 20% (6/30) (ns)</li> </ul> <p><b><u>Employed (part-time or full-time) (% of patients eligible for employment)<sup>††</sup></u></b></p> <ul style="list-style-type: none"> <li>• Baseline: 65% (11/17) versus 59% (10/17) (<math>P = \text{NR}</math>)</li> <li>• 12 months: 86% (18/21) versus 100% (22/22) (<math>P = \text{NR}</math>)</li> </ul> <p><b><u>Total relief with sequential procedures (weeks) (mean)</u></b></p> <ul style="list-style-type: none"> <li>• Overall total relief for 12 months: (n = 60) <math>48 \pm 6.2</math> versus (n = 60) <math>46 \pm 10.2</math> (ns)</li> <li>• Injection #1: (n = 2) 52 versus (n = 3) <math>30 \pm 19.9</math> (ns)</li> <li>• after 2<sup>nd</sup> injection: (n = 9) <math>43 \pm 10.8</math> versus (n = 7) <math>40.4 \pm 19.9</math> (ns)</li> </ul>	
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				<ul style="list-style-type: none"> <li>• after 3<sup>rd</sup> injection: (n = 14) 47 ± 6.7 versus (n = 14) 47 ± 6.5 (ns)</li> <li>• after 4<sup>th</sup> injection: (n = 31) 50 ± 3.5 versus (n = 27) 48 ± 6.5 (ns)</li> <li>• after 5<sup>th</sup> injection: (n = 4) 51 ± 2.0 versus (n = 9) 52 ± 0 (ns)</li> </ul> <p><b><u>Average relief per procedure (weeks)</u></b></p> <ul style="list-style-type: none"> <li>• Overall relief per procedure: (n = 60) 16 ± 7.9 versus (n = 60) 14 ± 6.9 (ns)</li> <li>• Injection #1: (n = 2) 52 versus (n = 3) 30 ± 19.9 (ns)</li> <li>• after 2<sup>nd</sup> injection: (n = 9) 22 ± 5.4 versus (n = 7) 20 ± 9.9 (ns)</li> <li>• after 3<sup>rd</sup> injection: (n = 14) 16 ± 2.2 versus (n = 14) 16 ± 2.2 (ns)</li> <li>• after 4<sup>th</sup> injection: (n = 31) 12 ± 0.9 versus (n = 27) 12 ± 1.6 (ns)</li> <li>• after 5<sup>th</sup> injection: (n = 4) 10 ± 0.4 versus (n = 9) 10 ± 0 (ns)</li> </ul>		
<b>Barnsley, 1994<sup>15</sup></b>	<p><b>RCT</b></p> <p>N = 42</p> <p>CNP of facet joint origin</p> <p>Chronic (≥ 3 months)</p> <p>Mean age (± SD): 43.0 ± 10.5 years†</p> <p>61% female†</p>	<p>1, 2, 4, 8, 12, 16, 20, 36 weeks: (98% f/u at all followups; 41/42)</p>	<p>medial branch block (fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone (5.7 mg)</p> <p><u>Repeat injections:</u> 1 injection given to each patient</p> <p><u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)</p>	<p><b>Medial branch block steroid/local anesthetic (n = 21) versus local anesthetic injection (n = 20) (mean scores)</b></p> <p><b><u>Pain: median time to return to 50% of baseline pain levels (days):</u></b></p> <ul style="list-style-type: none"> <li>• 3 versus 3.5 days (ns)</li> </ul>	Grant received from Motor Accidents Authority of New South Wales, Australia	IIb

CNP: cervical neck pain

CMM: conservative medical management

f/u: follow-up

LoE: level of evidence

NRS: Numerical Rating Scale

ns: not statistically significant

NR: not reported

NDI: Neck Disability Index

MPQ: McGill Pain Questionnaire

SCL: Symptom Checklist

\*This report states the original patient assignments as follows: 30 patients within each treatment subgroup (steroid/anesthetic or steroid/anesthetic plus Sarapin) and 30 patients within each control subgroup (anesthetic or anesthetic plus Sarapin) for a total sample size of 120 patients. No significant differences in any outcome measure were found between the Sarapin and non-Sarapin groups, so all results are reported for treatment (steroid + anesthetic) versus control (anesthetic only) [Manchikanti, 2008 Cervical Medial Branch Blocks]. An earlier report of this study [Manchikanti, 2006] presents a sub-analysis of 60 patients for the outcomes, comparing 15 patients within each treatment subgroup (steroid/anesthetic or steroid/anesthetic plus Sarapin) and 15 patients within each control subgroup (anesthetic or anesthetic plus Sarapin).

†Data represents only patients with complete follow-up [Manchikanti, 2008 Cervical Medial Branch Blocks; Barnsley, 1994].

‡ Data carried forward: if a patient is lost to follow-up or unblinded (and hence withdrawn), Manchikanti's studies carries that patient's last available data forward to all subsequent data points. Thus, it appears that each follow-up has data for all patients available but often some of the data has actually been carried forward from the last available data point. Data from any follow-up in which < 20% of the data in either group was carried forward will not be included in our analysis.

§ The pain relief results are as reported in an earlier report of this study by averaging the results within each treatment (steroid/anesthetic and steroid/anesthetic plus Sarapin) and control subgroups (anesthetic and anesthetic plus Sarapin). Note that each treatment group comprises 30 patients [Manchikanti, 2006].

\*\* The opioid intake results are reported in an earlier report of this study for 60 patients and are defined as: mild intake (Schedule IV opioids such as hydrocodone 2 times/day or less), moderate intake (Schedule III opioids such as hydrocodone up to 4 times/day), and heavy intake (Schedule II opioids such as oxycodone or morphine in any dose) [Manchikanti, 2006].

†† Employment status was determined at the time of enrollment. Employable category includes patients unemployed or employed on a part-time basis with limited or no employment due to pain [Manchikanti, 2008, Cervical Medial Branch Blocks].

### Appendix Q. Safety data from RCTs: lumbar spinal injections

Author (Year)	Study type  No. patients randomized (N) Diagnosis Duration of symptoms Mean age (range) Sex	Duration of follow-up (% complete follow-up rate) (no. of injections)	Interventions	Complications
<b>Manchikanti (2008, pt 2)<sup>132</sup></b>	<b>RCT</b>  N = 120  LBP due to disc herniation and radiculitis  Chronic ( $\geq 6$ months)  Mean age ( $\pm$ SD): 47.1 $\pm$ 14.9* years  67% female*	3 months: 46% (82/180)  6 months: 43% (77/180)  12 months: 41% (74/180)  % patients with data carried forward (steroid vs control):  3 months: 2% (1/42) vs 2% (1/42)  6 months: 7% (3/42) vs 10% (4/42)  12 months: 10% (4/42) vs 14% (6/42)	Caudal epidural (fluoroscopy guidance)  <u>Steroids used:</u> Betamethasone (6 mg) <u>OR</u> methylprednisone (40 mg)  <u>Repeat injections:</u> as needed with increasing pain (mean: 3.8 $\pm$ 1.2 injections/year)  <u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)	<ul style="list-style-type: none"> <li>• no major adverse events reported within 1 year.</li> <li>• weight gain (mean lbs <math>\pm</math> SD): tx (n = 42) versus control (n = 42) <ul style="list-style-type: none"> <li>• baseline (mean): 180.7 <math>\pm</math> 44.0 versus 204.8 <math>\pm</math> 53.1 (<math>P = .027</math>)</li> <li>• 12 months (mean): 178.7 <math>\pm</math> 44.4 versus 198.7 <math>\pm</math> 60.0 (ns)</li> <li>• weight loss (% patients): 64% (27/42) versus 57% (24/42) (ns)</li> <li>• weight gain (% patients): 24% (10/42) versus 24% (10/42) (ns)</li> </ul> </li> </ul>

<p><b>Manchikanti (2010)<sup>136</sup></b> Evaluation of the effectiveness</p>	<p><b>RCT</b></p> <p>N = 120</p> <p>LBP due to disc herniation and radiculitis</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): 42.0 <math>\pm</math> 11.8* years</p> <p>66% female†</p>	<p>3 months: 57% (68/120)</p> <p>6 months: 53% (64/120)</p> <p>12 months: 50% (60/120)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 0% (0/35) vs 6% (2/35)</p> <p>6 months: 6% (2/35) vs 11% (4/35)</p> <p>12 months: 9% (3/35) vs 20% (7/35)</p>	<p>Interlaminar epidural (fluoroscopy guidance); 91% between L5 and S1, 7% between L4 and L5, and 2% at other levels</p> <p><u>Steroids used:</u> Betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: <math>\pm</math> injections/year)</p> <p><u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• dural puncture: 1/283 injections</li> <li>• headache (secondary to puncture): 0/283 injections</li> <li>• nerve root irritation: 0/283 injections</li> <li>• major adverse events (not specified): 0/283 injections</li> <li>• weight gain (mean lbs <math>\pm</math> SD): tx (n = 35) versus control (n = 35) <ul style="list-style-type: none"> <li>• baseline (mean): 179.4 <math>\pm</math> 48.2 versus 211.7 <math>\pm</math> 54.9 (<math>P = .011</math>)</li> <li>• 12 months (mean): 177.1 <math>\pm</math> 48.8 versus 208.3 <math>\pm</math> 56.6 (<math>P = .016</math>)</li> <li>• weight loss (% patients): 57% (20/35) versus 54% (19/35) (<math>P = \text{NR}</math>)</li> <li>• weight gain (% patients): 34% (12/35) versus 26% (9/35) (<math>P = \text{NR}</math>)</li> </ul> </li> </ul>
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<p><b>Manchikanti (2008, pt 1)<sup>118</sup></b></p>	<p><b>RCT</b></p> <p>N = 120</p> <p>LBP without disc herniation or radiculitis, based on controlled facet joint nerve blocks</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): 46.0 <math>\pm</math> 14.6* years</p> <p>60% female*</p>	<p>3 months: 59% (71/120)</p> <p>6 months: 57% (68/120)</p> <p>12 months: 52% (62/120)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 3% (1/36) vs 0% (0/36)</p> <p>6 months: 3% (1/36) vs 8% (3/36)</p> <p>12 months: 8% (3/36) vs 19% (7/36)</p>	<p>Caudal epidural (fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone (6 mg) <u>OR</u> methylprednisone (40 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: 3.8 <math>\pm</math> 1.2 injections/year)</p> <p><u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• no major adverse events reported within 1 year.</li> <li>• weight gain (mean lbs <math>\pm</math> SD): tx (n = 36) versus control (n = 36) <ul style="list-style-type: none"> <li>• baseline (mean): 187.8 <math>\pm</math> 41.3 versus 194.8 <math>\pm</math> 61.7 (ns)</li> <li>• 12 months (mean): 186.3 <math>\pm</math> 42.8 versus 191.6 <math>\pm</math> 60.0 (ns)</li> <li>• weight loss (% patients): 53% (19/36) versus 53% (19/36) (<math>P = \text{NR}</math>)</li> <li>• weight gain (% patients): 36% (13/36) versus 30% (11/36) (<math>P = \text{NR}</math>)</li> </ul> </li> </ul>
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<p><b>Manchikanti (2010)<sup>116</sup></b> Preliminary Results of a Randomized</p>	<p><b>RCT</b></p> <p>N = 120</p> <p>LBP without disc herniation or radiculitis, based on controlled facet joint nerve blocks</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): 41.8 <math>\pm</math> 12.2* years</p> <p>67% female*</p>	<p>3 months: 57% (57/120)</p> <p>6 months: 53% (64/120)</p> <p>12 months: 49% (59/120)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 3% (1/35) vs 3% (1/35)</p> <p>6 months: 9% (3/35) vs 9% (3/35)</p> <p>12 months: 20% (7/35) vs 11% (4/35)</p>	<p>Interlaminar epidural (fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: 3.9 <math>\pm</math> 1.1 injections/year)</p> <p><u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• nerve root irritation: NR</li> <li>• headache, for 3 days postop (without dural puncture: 1/267 injections</li> <li>• weight gain secondary to high dose steroid for unrelated medical problem: 1/267 injections</li> <li>• major adverse events (not specified): NR</li> <li>• weight gain (mean lbs <math>\pm</math> SD): tx (n = 35) versus control (n = 35) <ul style="list-style-type: none"> <li>• baseline (mean): 169.0 <math>\pm</math> 44.9 versus 215.6 <math>\pm</math> 53.1 (<math>P = .000</math>)</li> <li>• 12 months (mean): 166.5 <math>\pm</math> 45.2 versus 215.6 <math>\pm</math> 56.6 (<math>P = .000</math>)</li> <li>• weight loss (% patients): 54% (19/35) versus 40% (14/35) (<math>P = \text{NR}</math>)</li> <li>• weight gain (% patients): 31% (11/35) versus 43% (15/35) (<math>P = \text{NR}</math>)</li> </ul> </li> <li>• subarachnoid puncture: 1/267 injections <ul style="list-style-type: none"> <li>• headache (secondary to puncture): 0/267 injections</li> </ul> </li> </ul>
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<p><b>Manchikanti (2008, pt 4)<sup>115</sup></b></p>	<p><b>RCT</b></p> <p>N = 61</p> <p>LBP due to spinal stenosis with radiculitis</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): 60.4 <math>\pm</math> 15.8* years</p> <p>70% female*</p>	<p>3 months: 59% (36/61)</p> <p>6 months: 49% (30/61)</p> <p>12 months: 46% (28/61)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 15% (3/20) vs 5% (1/20)</p> <p>6 months: 25% (5/20) vs 25% (5/20)</p> <p>12 months: 25% (5/20) vs 35% (7/20)</p>	<p>Caudal epidural (fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: 3.0 <math>\pm</math> 1.2 injections/year)</p> <p><u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• no major adverse events reported within 1 year.</li> <li>• weight gain (mean lbs <math>\pm</math> SD): tx (n = 20) versus control (n = 20) <ul style="list-style-type: none"> <li>• baseline (mean): 192 <math>\pm</math> 59.0 versus 186 <math>\pm</math> 55.2 (ns)</li> <li>• 12 months (mean): 189 <math>\pm</math> 59.7 versus 183 <math>\pm</math> 56.0 (ns)</li> </ul> </li> <li>• weight loss (% patients): NR</li> <li>• weight gain (% patients): NR</li> </ul>
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<p><b>Sayegh (2009)<sup>176</sup></b></p>	<p><b>RCT</b></p> <p>N = 183</p> <p>LBP with disc herniation or radiculitis, based on MRI scan</p> <p>Chronic (<math>\geq 1</math> month)</p> <p>Mean age (<math>\pm</math> SD): 49.3 <math>\pm</math> 15.6 years</p> <p>33% female</p>	<p>1 week: (100% f/u; 183/183)</p> <p>1 month: (95% f/u; 174/183)</p> <p>6 months: (84% f/u; 153/183)</p> <p>12 months: (83% f/u; 151/183)</p>	<p>Caudal epidural (<u>without</u> fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone dipropionate (1 mL) and betamethasone phosphate ((2+5) mg/dL)</p> <p><u>Repeat injections:</u> as needed if ODI and SLR test did not improve; 28% (51/183) patients received 2<sup>nd</sup> injection</p> <p><u>Cointerventions:</u> Pts allowed to receive paracetamol during first 4 weeks of study, but not non-steroid anti-inflammatory meds</p>	<ul style="list-style-type: none"> <li>• subarachnoid puncture: NR</li> <li>• nerve root irritation: NR</li> <li>• transient bilateral lower extremity numbness immediately postop: 20/183 patients</li> <li>• possible fainting (bp and pulse normal): 12/183 patients</li> <li>• lower limb dysfunction (loss of sensation and/or reduced motor power, or bladder and bowel dysfunction): 0/183 patients</li> <li>• major adverse events (not specified): 0/183 patients</li> <li>• weight gain: NR</li> </ul>
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<p><b>Manchikanti (2008, pt 3)<sup>133</sup></b></p>	<p><b>RCT</b></p> <p>N = 68</p> <p>LBP due to post lumbar surgery syndrome</p> <p>Chronic (<math>\geq 6</math> months after previous lumbar surgery)</p> <p>Mean age (<math>\pm</math> SD): 53.1 <math>\pm</math> 13.0* years</p> <p>55% female*</p>	<p>3 months: 54% (37/68)</p> <p>6 months: 47% (32/68)</p> <p>12 months: 38% (26/68)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 10% (2/20) vs 5% (1/20)</p> <p>6 months: 25% (5/20) vs 15% (3/20)</p> <p>12 months: 35% (7/20) vs 35% (7/20)</p>	<p>Caudal epidural (fluoroscopy guidance)</p> <p><u>Steroids used:</u> betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: 3.4 <math>\pm</math> 1.3 injections/year)</p> <p><u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• no major adverse events reported within 1 year</li> <li>• weight gain (mean lbs <math>\pm</math> SD): tx (n = 20) versus control (n = 20) <ul style="list-style-type: none"> <li>• baseline (mean): 187 <math>\pm</math> 56.2 versus 193 <math>\pm</math> 53.9 (ns)</li> <li>• 12 months (mean): 183 <math>\pm</math> 55.2 versus 189 <math>\pm</math> 49.8 (ns)</li> <li>• weight loss (% patients): 65% (13/20) versus 50% (10/20) (<math>P = \text{NR}</math>)</li> <li>• weight gain (% patients): 20% (4/20) versus 25% (5/20) (<math>P = \text{NR}</math>)</li> </ul> </li> </ul>
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<p><b>Manchikanti (2009)<sup>117</sup></b> Preliminary Results of a Comparative</p>	<p><b>RCT</b></p> <p>N = 82</p> <p>LBP due to spinal stenosis with radiculitis</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): <math>61.5 \pm 13.2^*</math> years</p> <p>58% female*</p>	<p>3 months: 61% (50/82)</p> <p>6 months: 49% (40/82)</p> <p>12 months: 39% (32/82)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 0% (0/25) vs 0% (0/25)</p> <p>6 months: 40% (10/25) vs 0% (0/25)</p> <p>12 months: 72% (18/25) vs 0% (0/25)</p>	<p>Percutaneous epidural adhesiolysis (fluoroscopy and lumbar epidurogram guidance) ‡</p> <p><u>Steroids used</u> (both treatment and control groups): betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: <math>2.7 \pm 0.9</math> injections/year)</p> <p><u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• subarachnoid placement of catheter with no resulting complications: 1/25 patients in adhesiolysis group</li> <li>• death due to problems unrelated to study in epidural group: 1/25</li> <li>• weight gain: NR</li> </ul>
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<p><b>Manchikanti (2009)<sup>134A</sup></b> Comparative Effectiveness Evaluation</p>	<p><b>RCT</b></p> <p>N = 180</p> <p>LBP due to post lumbar surgery syndrome</p> <p>Chronic (<math>\geq 6</math> months after previous lumbar surgery)</p> <p>Mean age (<math>\pm</math> SD): <math>52 \pm 13.2^*</math> years</p> <p>58% female*</p>	<p>3 months: 67% (120/180)</p> <p>6 months: 61% (109/180)</p> <p>12 months: 41% (74/180)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 0% (0/60) vs 0% (0/60)</p> <p>6 months: 40% (10/60) vs 2% (1/60)</p> <p>12 months: 72% (43/60) vs 5% (3/60)</p>	<p>Percutaneous epidural adhesiolysis (fluoroscopy and lumbar epidurogram guidance) ‡</p> <p><u>Steroids used</u> (both treatment and control groups): betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain after at least 3 months (mean: <math>2.9 \pm 1.1</math> injections/year)</p> <p><u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>no major adverse events reported within 1 year</li> </ul>
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<p><b>Koc (2009)<sup>99</sup></b></p>	<p><b>RCT</b></p> <p>N = 33</p> <p>LBP due to spinal stenosis</p> <p>Chronic (mean duration of symptoms: <math>5.4 \pm 5.6</math> years)*</p> <p>Mean age (<math>\pm</math> SD): <math>59 \pm 10.8^*</math> years</p> <p>72% female*</p>	<p>2 wks, and 1, 3 months (% f/u: NR)</p> <p>6 months(88% f/u; 29/33)</p>	<p>Interlaminar epidural (through the most stenotic level under fluoroscopy guidance)</p> <p><u>Steroids used</u> triamcinolon acetonide (60 mg)</p> <p><u>Repeat injections:</u> (mean injections/year: NR)</p> <p><u>Cointerventions:</u> all patients performed home-based therapeutic exercise program and received oral diclofenac sodium, 2 doses/day/2 weeks</p>	<ul style="list-style-type: none"> <li>• weight gain NR</li> <li>• gastric complaints: 1/33 patients</li> <li>• angina pectoris: 1/33 patients</li> <li>• major adverse events (not specified): NR</li> </ul>
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<p><b>Ghahreman (2010)<sup>64</sup></b></p>	<p><b>RCT</b></p> <p>N = 150</p> <p>Lumbar radicular pain</p> <p>Acute (n = 80) or chronic (n = 70): <u>Acute</u>: median duration of symptoms: 6 weeks <u>Chronic</u>: median duration of symptoms: 54 weeks</p> <p>Mean age: 46.1 years</p> <p>59.3% male</p>	<p>1 month (100% f/u, 150/150) (primary f/u)</p> <p>***</p> <p><b>Once pts registered as having failed the treatment (pain relief &lt; 50% and registered their f), they were no longer followed.</b></p> <p>Patients were followed as long as they had a successful outcome.</p> <p>3-12 months (<math>\leq 23\%</math> f/u (34/150))</p>	<p>Transforaminal epidural (fluoroscopy guidance)</p> <p><u>Steroids used</u>: Triamcinolone (70 mg)</p> <p><u>Repeat injections</u>: at discretion of patient up to 3 injections (mean of 1.1 injections/pt as calculated by RH; no patient required more than 2 injections)</p> <p><u>Cointerventions</u>: not restricted; all cointerventions reported</p>	<ul style="list-style-type: none"> <li>• none attributed to treatment</li> </ul>
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<p><b>Tafazal (2009)</b><sup>197</sup></p>	<p><b>RCT</b></p> <p>N = 150</p> <p>LBP with disc herniation or foraminal stenosis</p> <p>Chronic (mean duration of symptoms: 18.9 months, interquartile range: 6 – 24.5 months)</p> <p>Mean age: 51.9 years</p> <p>35% female</p>	<p>6 weeks: 94% (141/150)</p> <p>3 months: 83% (124/150)**</p> <p>12 months (median 20 months, range 12 – 31)</p> <p>86% (129/150)</p>	<p>Transforaminal (peri-radicular) epidural (fluoroscopy guidance)</p> <p><u>Steroids used:</u> Methylprednisolone (depomedrone) (40 mg)</p> <p><u>Repeat injections:</u> (none) as needed with based on significant residual leg pain after at least 12 months (mean injections/year NR)</p> <p><u>Cointerventions:</u> patients agreed not to alter oral analgesic medication and had no additional treatments, such as physical therapy, during study periods</p>	<ul style="list-style-type: none"> <li>major adverse events (not specified): 0/150 patients</li> <li>death (cause not specified): 2/150 patients</li> </ul>
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<p><b>Manchikanti (2010)<sup>135§</sup></b> Evaluation of Lumbar Facet</p>	<p><b>RCT</b>  N = 120  LBP of facet joint origin  Chronic (<math>\geq 6</math> months)  Mean age (<math>\pm</math> SD): 47 <math>\pm</math> 16* years  60% female*</p>	<p>3 months: 98% (118/120)  6 months: 92% (110/120)  12 months: 83% (99/120)  18 months: 73% (88/120)  24 months: 80% (96/120)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 0% (0/60) vs 3% (2/60)  6 months: 5% (3/60) vs 12% (7/60)  12 months: 20% (12/60) vs 15% (9/60)  18 months: 28% (17/60) vs 20% (15/60)  24 months: 20% (12/60) vs 20% (12/60)</p>	<p>Facet joint nerve block (fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone (0.075 – 0.225 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: 5 – 6 injections/24 months)</p> <p><u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>no major adverse events reported within 1 year.</li> </ul>
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<b>Peng (2010)<sup>161</sup></b>	<b>RCT</b>  N = 72  LBP without radiculopathy and with lumbar disc degeneration  Chronic (mean duration 3.4 ±1.7 years)  Mean age (± SD): 42 ± 13.3 years  43% female	6, 12, 24 months(98.6% f/u; 71/72)	lumbar intradiscal(under fluoroscopy guidance)  <u>Steroids used</u> none Treatment: Methylene blue (10 mg)  <u>Repeat injections:</u> (mean injections/year NR)  <u>Cointerventions:</u> bedrest for 24 hours and patients asked to avoid strenuous exercise for 3 weeks	<ul style="list-style-type: none"> <li>• nerve root injury: 0/36 patients in treatment group</li> <li>• back pain aggravation: 0/36 patients in treatment group</li> <li>• disc space infection: 0/72 patients</li> <li>• nerve root stab injury: 0/72 patients</li> <li>• major adverse events (not specified): NR</li> </ul>
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CMM: conservative medical management

f/u: follow-up

LBP: low back pain

NR: not reported

ns: not statistically significant

SD: standard deviation

tx: treatment

bp: blood pressure

\* Data represents only patients with complete follow-up [Manchikanti, 2008 pt 1, 2, 3, and 4; Manchikanti, 2010, Evaluation of the effectiveness; Manchikanti, 2010, Preliminary Results of a Randomized, Double-blind; Manchikanti, 2009, Preliminary Results of a Comparative; Koc, 2009; Manchikanti, 2009, Comparative Effectiveness; Murata, 2009; Manchikanti, 2010, Evaluation of Lumbar Facet]

†Error in reporting the number of females in Group 1 in Table 1: article reports a total of 42 males and females with a total sample size of 35 [Manchikanti, 2010, Evaluation of the effectiveness...].

‡ Treatment procedure:

- Treatment group: targeted adhesiolysis, lidocaine + 10% saline + steroid + normal saline [Manchikanti, 2009, Preliminary Results of a Comparative; Manchikanti, 2009, A Comparative Effectiveness Evaluation]. Lidocaine + steroid in L2 [Murata, 2009].
- Control group: non-targeted catheter up to S3, lidocaine + normal saline + steroid + normal saline [Manchikanti, 2009, Preliminary Results of a Comparative].
- Control group: non-targeted catheter up to S3, lidocaine + 0.9% saline + steroid + normal saline (note: this is the procedure reported in the narration, which differs from Table 1 (control group reported to receive “normal saline” rather than 0.9% saline) [Manchikanti, 2009, A Comparative Effectiveness Evaluation].
- Control group: lidocaine + steroid in back muscle in same area as L2 [Murata, 2009].

§The treatment and control groups were initially subdivided further into 2 groups: anesthetic + Sarapin (n = 30) and anesthetic + Sarapin (n = 30). No significant differences were found between the subgroups on any outcome, so all results are reported for major group: treatment (steroid + anesthetic) versus control (anesthetic only) [Manchikanti, 2010, Evaluation of Lumbar Facet].

\*\*Inconsistency in reporting follow-up. The author reported that 141 patients were available at the 6 week follow-up and 16 patients who did not attend 3 month follow-up, giving a total of 124 patients at the follow-up. Either 17 patients did not attend the 3 month follow-up or the number of patients at 3 month-follow-up should total 125 [Tafazal, 2009].

**Appendix R. Safety data from RCTs: cervical spinal injections**

Author (Year)	Study type  No. patients randomized (N) Diagnosis Duration of symptoms Mean age (range) Sex	Duration of f/u (% complete f/u rate)	Interventions	Complications
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<p><b>Manchikanti (2010)<sup>124</sup></b> Cervical Epidural Injections</p>	<p><b>RCT</b></p> <p>N = 120</p> <p>CNP without disc herniation or radiculitis</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): 44.5 <math>\pm</math> 12.0* years</p> <p>66% female*</p>	<p>3 months: 58% (70/120)</p> <p>6 months: 57% (68/120)</p> <p>12 months: 56% (67/120)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 0% (0/35) vs 0% (0/35)</p> <p>6 months: 3% (1/35) vs 3% (1/35)</p> <p>12 months: 6% (2/35) vs 3% (1/35)</p>	<p>Interlaminar epidural (fluoroscopy guidance); 27% between T1/C7; 64% between C6/ C7; 9% between C5/C6</p> <p><u>Steroids used:</u> Betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: 3.9 <math>\pm</math> 1.0 injections/year)</p> <p><u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• subarachnoid puncture: 0/262 injections</li> <li>• nerve root irritation (received 8 mg Decadron, no long-term complications): 3/262 injections</li> <li>• major adverse events (not specified): NR</li> <li>• weight gain (mean lbs <math>\pm</math> SD): tx (n = 35) versus control (n = 35) <ul style="list-style-type: none"> <li>• baseline (mean): 179.6 <math>\pm</math> 40.9 versus 174.2 <math>\pm</math> 50.6 (ns)</li> <li>• 12 months (mean): 177.9 <math>\pm</math> 43.1 versus 173.3 <math>\pm</math> 53.8 (ns)</li> <li>• weight loss (% patients): 46% (16/35) versus 43% (15/35) (ns)</li> <li>• weight gain (% patients): 40% (14/35) versus 34% (12/35) (ns)</li> </ul> </li> </ul>
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<p><b>Manchikanti (2010)<sup>125</sup></b> Effectiveness of Fluoroscopic</p>	<p><b>RCT</b></p> <p>N = 120</p> <p>CNP with disc herniation and radiculitis</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): 46.1 <math>\pm</math> 10.6* years</p> <p>64% female*</p>	<p>3 months: 58% (70/120)</p> <p>6 months: 57% (68/120)</p> <p>12 months: 56% (67/120)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 0% (0/35) vs 0% (0/35)</p> <p>6 months: 3% (1/35) vs 3% (1/35)</p> <p>12 months: 6% (2/35) vs 3% (1/35)</p>	<p>Interlaminar epidural (fluoroscopy guidance); 31% between T1/C7; 60% between C6/ C7; 9% between C5/C6</p> <p><u>Steroids used:</u> Betamethasone (6 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: 3.7 <math>\pm</math> 1.2 injections/year)</p> <p><u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>• subarachnoid puncture (1000 mg caffeine infusion, no subsequent headache): 3/262 injections</li> <li>• nerve root irritation (received 8 mg Decadron, no long-term complications): 3/262 injections</li> <li>• major adverse events (not specified): NR</li> <li>• weight gain (mean lbs <math>\pm</math> SD): tx (n = 35) versus control (n = 35) <ul style="list-style-type: none"> <li>• baseline (mean): 168.2 <math>\pm</math> 42.2 versus 186.5 <math>\pm</math> 46.3 (ns)</li> <li>• 12 months (mean): 167.8 <math>\pm</math> 43.2 versus 185.5 <math>\pm</math> 58.7 (ns)</li> <li>• weight loss (% patients): 49% (17/35) versus 37% (13/35) (ns)</li> <li>• weight gain (% patients): 37% (13/35) versus 40% (14/35) (ns)</li> </ul> </li> </ul>
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<p><b>Stav (1993)<sup>193</sup></b></p>	<p><b>RCT</b></p> <p>N = 50†</p> <p>CNP with resistant cervicobrachialgia</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): 51.1 <math>\pm</math> 2.7* years</p> <p>55% female*</p>	<p>1 week, 12 months: (84% f/u; 42/50)</p>	<p>Cervical epidural(<u>no</u> fluoroscopy guidance);into C5-C6 or C6-C7 interspace</p> <p><u>Steroids used:</u> Methylprednisolone sodium acetate (80 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain at 2 week intervals (mean: 2.5 <math>\pm</math> 0.16 injections)</p> <p><u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>major adverse events (not specified): 0/42 patients</li> </ul>
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<p><b>Manchikanti (2008)</b><sup>137</sup>‡ Cervical Medial Branch Blocks <b>Manchikanti, (2006)</b><sup>126</sup></p>	<p><b>RCT</b></p> <p>N = 120</p> <p>CNP of facet joint origin</p> <p>Chronic (<math>\geq 6</math> months)</p> <p>Mean age (<math>\pm</math> SD): 44.5 <math>\pm</math> 13.5* years</p> <p>74% female*</p>	<p>3 months: 98% (118/120)</p> <p>6 months: 93% (111/120)</p> <p>12 months: 88% (106/120)</p> <hr/> <p>% patients with data carried forward (steroid vs control):</p> <p>3 months: 2% (1/60) vs 2% (1/60)</p> <p>6 months: 8% (5/60) vs 7% (4/60)</p> <p>12 months: 10% (6/60) vs 13% (8/60)</p>	<p>medial branch block(fluoroscopy guidance)</p> <p><u>Steroids used:</u> Betamethasone (0.075 – 0.225 mg)</p> <p><u>Repeat injections:</u> as needed with increasing pain (mean: 3.5 <math>\pm</math> 1.0 injections/year)</p> <p><u>Cointerventions:</u> not required/ uncontrolled (CMM by patient choice)</p>	<ul style="list-style-type: none"> <li>no major adverse events reported within 1 year.</li> </ul>
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<b>Barnsley, (1994)<sup>15</sup></b>	<b>RCT</b>  N = 42  CNP of facet joint origin  Chronic ( $\geq 3$ months)  Mean age ( $\pm$ SD): 43.0 $\pm$ 10.5 years*  61% female*	1, 2, 4, 8, 12, 16, 20, 36 weeks: (98% f/u at all followups; 41/42)	medial branch block (fluoroscopy guidance)  <u>Steroids used:</u> Betamethasone (5.7 mg)  <u>Repeat injections:</u> 1 injection given to each patient  <u>Cointerventions:</u> not required/uncontrolled (CMM by patient choice)	<ul style="list-style-type: none"> <li>• transient facial flushing (2/41)</li> <li>• temporary exacerbation of usual when analgesic effect worn off (NR)</li> <li>• major adverse events (not specified): NR</li> </ul>
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CNP: cervical neck pain

CMM: conservative medical management

f/u: follow-up

NR: not reported

ns: not statistically significant

SD: standard deviation

tx: treatment

\*Data represents only patients with complete follow-up [Manchikanti, 2010 Cervical Epidural Injections; Manchikanti, 2010, Effectiveness of Fluoroscopic; Manchikanti, 2008, Cervical Medial Branch Block; Manchikanti, 2006; Barnsley, 1994] or for most patients with follow-up (n = 40) [Stav, 1993].

†Five patients in each group started placebo treatment (posterior intramuscular injection) during initial exam, then received treatment per randomization [Stav, 1993].

‡This report states the original patient assignments as follows: 30 patients within each treatment subgroup (steroid/anesthetic or steroid/anesthetic plus Sarapin) and 30 patients within each control subgroup (anesthetic or anesthetic plus Sarapin) for a total sample size of 120 patients. No significant differences in any outcome measure were found between the Sarapin and non-Sarapin groups, so all results are reported for treatment (steroid + anesthetic) versus control (anesthetic only) [Manchikanti, 2008 Cervical Medial Branch Blocks]. An earlier report of this study [Manchikanti, 2006] presents a sub-analysis of 60 patients for the outcomes, comparing 15 patients within each treatment subgroup (steroid/anesthetic or steroid/anesthetic plus Sarapin) and 15 patients within each control subgroup (anesthetic or anesthetic plus Sarapin).

**Appendix S. Safety data from non-randomized studies with  $\geq 100$  patients.**

Author (Year)	Study type  Sample size (N)  Diagnosis Duration of symptoms Mean age (range) Sex	Duration of follow-up (% complete follow-up rate)	Interventions	Complications
Lumbar				

<p><b>Botwin (2000)</b></p>	<p>Case series (retrospective)</p> <p>N = 235 (322 injections)*</p> <p>LBP and radicular pain due to HNP or LSS</p> <p>Duration of pain (mean): 35 months* (range NR)</p> <p>Mean age: 65.4 years* (range, 17-91 years)</p> <p>53% male*</p>	<p>24 hours, 1-3 weeks (59% f/u; 207/350 (no. of consecutive charts reviewed for potential inclusion)</p>	<p>Transforaminal epidural injection (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Betamethasone acetate (9-12 mg) <u>OR</u> methylprednisone sodium succinate (80 mg)</p> <p><u>Repeat injections:</u> 1-3 injections (mean: 1.6 injections)</p> <p><u>Cointerventions:</u> Anti-inflammatory analgesics and physical therapy referral</p>	<ul style="list-style-type: none"> <li>• <b>Overall complication rate:</b> 9.6% (31 complications/322 injections) (<math>\leq 1</math> per injection)</li> <li>• <b>Headaches</b> <ul style="list-style-type: none"> <li>• Transient/ nonpositional, resolved in 24 hours: 4.8% patients (10/207); 3.1% injections (10/322 injections)</li> <li>• Dural puncture: n/a</li> </ul> </li> <li>• <b>Dural puncture:</b> 0% injections/patients</li> <li>• <b>Pain at injection site</b> (increased back pain) (resolved in 24 hours): 3.9% patients (8/207); 2.4% injections (8/322)</li> <li>• <b>Increased leg pain</b> with radicular symptoms: 1.0% patients (2/207); 0.6% injections (2/322) <ul style="list-style-type: none"> <li>• Transient in one patient</li> <li>• Persistent pain until second injection 2 weeks later in other patient</li> </ul> </li> <li>• <b>Facial flushing</b> (transient, resolved in several days without treatment): 1.4% patients (3/207); 1.2% injections (4/322)</li> <li>• <b>Vasovagal reaction</b> (relieved with Trendelenburg positioning): 0.5% patients (1/207); 0.3% injections (1/322)</li> <li>• <b>Rash</b> (resolved by 2 weeks f/u): 0.5% patients (1/207); 0.3% injections (1/322)</li> <li>• <b>Leg weakness</b> (transient, resolved in 24 hours): 0.5% patients (1/207); 0.3% injections (1/322)</li> <li>• <b>Dizziness</b> (transient, resolved in 24 hours): 0.5% patients (1/207); 0.3% injections (1/322)</li> <li>• <b>Blood sugar elevation</b> (transient, resolved in 24 hours): 0.5% patients (1/207); 0.3% injections (1/322) (patient had insulin-dependent diabetes)</li> <li>• <b>Blood pressure elevation</b> (transient, resolved in 24 hours): 0.5% patients (1/207); 0.3% injections (1/322)</li> <li>• <b>Nausea</b> (transient, resolved in 24 hours): 0.5% patients (1/207); 0.3% injections (1/322)</li> </ul>
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<p><b>Botwin (2001)</b></p>	<p>Case series (retrospective)</p> <p>N = 139 (246 injections)</p> <p>LBP and radicular pain due to HNP or LSS</p> <p>Duration of pain (mean): 38 months* (range NR)</p> <p>Mean age: 64.3 years* (range, 36- 93 years)</p> <p>58% female*</p>	<p>24 hours, 1-3 weeks (85% f/u; 128/150† (no. of consecutive charts reviewed for potential inclusion)</p>	<p>Caudal epidural injection (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Betamethasone acetate (12 mg) <u>OR</u> triamcinolone acetate (80 mg)</p> <p><u>Repeat injections:</u> 1-3 injections (mean: 1.9 injections)</p> <p><u>Cointerventions:</u> Analgesics, anti- inflammatory medications and physical therapy referral</p>	<ul style="list-style-type: none"> <li>• <b>Overall complication rate:</b> 16.3% (40 complications/246 injections) (<math>\leq 1</math> per injection)</li> <li>• <b>Overall complications per injection:</b> <ul style="list-style-type: none"> <li>• #1: 15.1% (21/139 injections)</li> <li>• #2: 16.9% (14/83 injections)</li> <li>• #3: 14.3% (5/35)</li> </ul> </li> <li>• <b>Headaches</b> <ul style="list-style-type: none"> <li>• Transient/ nonpositional, resolved in 24 hours: 3.7% injections (9/246) (% patients NR)</li> <li>• Dural puncture: n/a</li> </ul> </li> <li>• <b>Dural puncture:</b> 0% injections/patients</li> <li>• <b>Pain at injection site</b> (increased back pain): 3.3% injections (8/246) (% patients NR)</li> <li>• <b>Increased leg pain</b> (transient, resolved in 24 hours): 0.8% patients (1/128); 0.4% injections (1/246)</li> <li>• <b>Facial flushing:</b> 2.4% injections (6/246)(% patients NR)</li> <li>• <b>Vasovagal reaction</b> (relieved with Trendelenburg positioning): 0.8% injections (2/246) (% patients NR)</li> <li>• <b>Insomnia</b> (night of procedure): 4.9% injections (12/246) (% patients NR)</li> <li>• <b>Nausea</b> (transient) 0.8% injections (2/246) (% patients NR)</li> </ul>
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<b>Candido 2010</b>	<p>Case series (retrospective)</p> <p>N = NR (7135 injections)</p> <p><b>Interlaminar (IL)</b> n = 4723 injections</p> <p><b>Transforaminal (TF)</b> n = 2412 injections</p> <p>chronic LBP with radicular symptoms</p> <p>Age, sex NR</p>	Procedural complications only	lumbar ESI (fluoroscopy guidance)	<ul style="list-style-type: none"> <li>• <b>Intradiscal injection:</b> 0.098% of injections (7/7135) <ul style="list-style-type: none"> <li>• Interlaminar approach: 0.021% of injections (1/4723)</li> <li>• Transforaminal approach: 0.249% of injections (6/2412)</li> </ul> </li> <li>• <b>Infection:</b> 0.0% injections (0/7135)</li> </ul>
<b>Everett (2004)</b>	<p>Case series (prospective)</p> <p>N = 240 (240 injections)</p> <p>Lumbar radicular or discogenic pain</p> <p>Duration of pain (mean): NR</p> <p>Mean age: NR</p> <p>Sex: NR</p>	2 days (% f/u NR)	<p>Transforaminal epidural injection (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Betamethasone acetate/Betamethasone sodium phosphate (6 mg) <u>OR</u> methylprednisolone (80 mg)</p> <p><u>Repeat injections:</u> none</p> <p><u>Cointerventions:</u> NR</p>	<ul style="list-style-type: none"> <li>• <b>Flushing</b> (defined as redness or warmth without rash): 11.3% patients (27/240); 11.3% injections (27/240)</li> </ul>

<p><b>Manchikanti (2004)</b> <b>Evaluation of lumbar...</b></p>	<p>Case series (prospective)</p> <p>N = 100 (256 injections)</p> <p>Low back pain due to disc degeneration, facet arthropathy, spinal stenosis, disc bulging, disc protrusion, disc herniation, epidural fibrosis, or no diagnosed abnormalities</p> <p>Duration of pain (mean): NR</p> <p>Mean age: NR</p> <p>60% female</p>	<p>Procedural, post-procedure, 24-72 hours (100% f/u)</p>	<p>Transforaminal epidural injection (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Betamethasone acetate/Betamethasone sodium phosphate (3-6 mg)</p> <p><u>Repeat injections:</u> none</p> <p><u>Cointerventions:</u> NR</p>	<ul style="list-style-type: none"> <li>• <b>Any complication (not including vascular puncture):</b> 7% patients (7/100)</li> <li>• <b>Soreness at injection site:</b> 6% patients (6/100)</li> <li>• <b>Increased pain:</b> 1% patients (1/100)</li> <li>• <b>Muscle spasms:</b> 1% patients (1/100)</li> <li>• <b>Swelling:</b> 0% patients (0/100)</li> <li>• <b>Headache:</b> 1% patients (1/100)</li> <li>• <b>Minor bleeding:</b> 0% patients (0/100)</li> <li>• <b>Dizziness:</b> 0% patients (0/100)</li> <li>• <b>Nausea/vomiting:</b> 1% patients (1/100)</li> <li>• <b>Fever:</b> 0% patients (0/100)</li> <li>• <b>Numbness:</b> 0% patients (0/100)</li> <li>• <b>Voiding difficulty:</b> 0% patients (0/100)</li> <li>• <b>Vasovagal reaction:</b> 0% patients (0/100)</li> <li>• <b>Motor weakness:</b> 0% patients (0/100)</li> <li>• <b>Insomnia:</b> 0% patients (0/100)</li> </ul> <p>No other complications were noted.</p>
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<p><b>Stalcup (2006)</b></p>	<p>Case series (retrospective)</p> <p>N = 1203 (1777 procedures (with one or more injection per procedure), 2217 injections)</p> <p>Diagnosis NR</p> <p>Duration of pain (mean): NR</p> <p>Mean age: 57.8 years (range NR)</p> <p>55.3% female</p>	<p>Procedural, immediate post-procedure (100% f/u)</p>	<p>Selective nerve root block (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Betamethasone acetate/Betamethasone sodium phosphate (dose NR) OR methylprednisolone acetate suspension (40 mg)</p> <p><u>Repeat injections:</u> Mean: 1.5 procedures per patient (range NR)</p> <p><u>Cointerventions:</u> NR</p>	<ul style="list-style-type: none"> <li>• <b>Any complication:</b> 5.5% procedures (98/1777) <ul style="list-style-type: none"> <li>• All resolved quickly with no prolonged damage/harm</li> </ul> </li> </ul> <p><b>Minor complications:</b></p> <ul style="list-style-type: none"> <li>• <b>Leg weakness OR lightheadedness:</b> 3.0% procedures (54/1777)</li> <li>• <b>Increased pain OR new pain:</b> 2.3% procedures (41/1777)</li> <li>• <b>Injection given at wrong vertebral level:</b> 0.06% procedures (1/1777) <ul style="list-style-type: none"> <li>• Error discovered while patient on operating table, and injection was given at the correct site; no adverse consequences</li> </ul> </li> </ul> <p><b>Major complications:</b></p> <ul style="list-style-type: none"> <li>• <b>Puncture of dural sac:</b> 0.06% procedures (1/1777) <ul style="list-style-type: none"> <li>• No lasting harm or increase follow-up care</li> </ul> </li> <li>• <b>Medication entered into subarachnoid space:</b> <ul style="list-style-type: none"> <li>• No lasting harm or increase follow-up care</li> </ul> </li> </ul> <p><b>Technical complications:</b></p> <ul style="list-style-type: none"> <li>• <b>Inability to localize needle tip properly, injection could not be given:</b> 0.4% procedures (7/1777)</li> </ul>
<p><b>Cervical</b></p>				

<p><b>Ma (2005)</b></p>	<p>Case series (retrospective)</p> <p>N = 844 (1036 injections)</p> <p>Disc herniation or foraminal stenosis</p> <p>Duration of symptoms: NR</p> <p>Mean age: 47 years (range NR)</p> <p>54% female</p>	<p>Immediate postprocedural data (100% f/u); patients instructed to call referring physicians if any side effects or complications occurred</p>	<p>Extraforaminal cervical nerve block (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Betamethasone acetate/Betamethasone sodium phosphate (6 mg) OR methylprednisolone acetate suspension (40 mg)</p> <p><u>Repeat injections:</u> Details NR</p> <p><u>Cointerventions:</u> NR</p>	<p><b><u>Minor complications:</u></b></p> <ul style="list-style-type: none"> <li>• <b>Any complication:</b> 1.7% patients (14/844), 1.64% injections (17/1036)</li> <li>• <b>Headache/dizziness:</b> 0.6% patients (5/844)</li> <li>• <b>Transient neurologic deficits (pain or weakness):</b> 0.7% patients (6/844)</li> <li>• <b>Hypersensitivity reaction:</b> 0.1% patients (1/844)</li> <li>• <b>Vasovagal reaction:</b> 0.1% patients (1/844)</li> <li>• <b>Transient global amnesia:</b> 0.1% patients (1/844)</li> </ul> <p><b><u>Major complications</u></b></p> <ul style="list-style-type: none"> <li>• <b>Death:</b> 0% patients (0/844)</li> <li>• <b>Paralysis:</b> 0% patients (0/844)</li> <li>• <b>Stroke:</b> 0% patients (0/844)</li> <li>• <b>Spinal cord injury:</b> 0% patients (0/844)</li> <li>• <b>Vertebral artery injury:</b> 0% patients (0/844)</li> <li>• <b>Infection:</b> 0% patients (0/844)</li> </ul> <p><b><u>Technical complications</u></b></p> <ul style="list-style-type: none"> <li>• <b>Wrong-site injection:</b> 0.4% patients (3/844) <ul style="list-style-type: none"> <li>• <b>wrong vertebral level:</b> 0.2% patients (2/844)</li> <li>• <b>wrong type of injection:</b> 0.1% patients (1/844) (facet block instead of nerve block)</li> <li>• no adverse consequences</li> <li>• not included in overall rate of any complications</li> </ul> </li> </ul>
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<p><b>Pobiel (2009)</b></p>	<p>Case series (prospective)</p> <p>N = 659 (802 injections)</p> <p>Cervical radiculopathy</p> <p>Duration of symptoms: NR</p> <p>Median age: 50 years (range, 25-89 years)</p> <p>62.8% male</p>	<p>Immediate postprocedural data (100% f/u); patients instructed to call referring physicians if any side effects or complications occurred in first week</p> <p>30 days: 52.4% (345/659; attempt to contact was only made in 460/659 patients)</p>	<p>Selective cervical nerve root blockade (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Betamethasone acetate/Betamethasone sodium phosphate (dose NR) OR methylprednisolone acetate suspension (dose NR) OR dexamethasone sodium phosphate (dose NR; particulate OR non-particulate formulations)</p> <p><u>Repeat injections:</u> 83 patients had repeat or alternate levels injected on a separate day</p> <p><u>Cointerventions:</u> NR</p>	<p><i>All complications were recorded 30 minutes postprocedure <u>unless otherwise noted.</u></i></p> <p><b><u>Minor complications:</u></b></p> <ul style="list-style-type: none"> <li>• <b>Any complication:</b> NR</li> <li>• <b>Vasovagal reaction:</b> 2.9% patients (19/659) (all responded to conservative treatments, including Trendelenburg positioning, cool compresses, or oral liquids)</li> <li>• <b>Sympathetic blockade:</b> 0.9% patients (6/659)</li> <li>• <b>Increase in usual pain:</b> <ul style="list-style-type: none"> <li>• <b>Immediate postprocedure:</b> 0.5% patients (3/659)</li> <li>• <b>30 days:</b> 2.0% patients (7/345)</li> </ul> </li> <li>• <b>Nausea:</b> 0.2% patients (1/659)</li> <li>• <b>Hematoma (suspected):</b> 0.2% patients (1/659) (resolved without sequelae)</li> <li>• <b>Minor allergic reaction:</b> 0.2% patients (1/659)</li> <li>• <b>Contralateral paresthesias:</b> 0.3% patients (1/345) (commenced 3 weeks following procedure, considered unrelated)</li> <li>• <b>Sensation of transient incomplete lung expansion:</b> 0.2% patients (1/659) (resolved without sequelae)</li> </ul> <p><b><u>Major complications</u></b></p> <ul style="list-style-type: none"> <li>• <b>Any major complication:</b> 0% patients (0/659)</li> </ul>
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<p><b>Schellhas (2007)</b></p>	<p>Case series (retrospective)</p> <p>N = 4612 (no. of injections NR)</p> <p>Cervical radiculopathy</p> <p>Duration of symptoms: NR</p> <p>Mean age: NR (range, 17-83 years)</p> <p>Sex: NR</p>	<p>Immediate postprocedural data (100% f/u); patients instructed to call referring physicians if any side effects or complications occurred in first week</p>	<p>Selective cervical nerve root blockade (anterolateral oblique approach) (therapeutic OR diagnostic) (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Betamethasone acetate suspension (dose NR) OR generic/formulated sodium phosphate or methylprednisolone phosphate or acetate (dose NR)</p> <p><u>Repeat injections:</u> NR</p> <p><u>Cointerventions:</u> NR</p>	<p><i>All complications were recorded 20-45 minutes postprocedure <u>unless otherwise noted.</u></i></p> <p><b><u>Minor complications:</u></b></p> <ul style="list-style-type: none"> <li>• <b>Any complication:</b> NR</li> <li>• <b>Increased clinical pain (≥ 10 days):</b> 10% of patients (patient number NR since complete f/u was only available immediately postprocedure</li> <li>• <b>Localized skin discoloration (≥ 14 days):</b> occurred in a “small number of patients (no exact count)”</li> </ul> <p><b><u>Major complications</u></b></p> <ul style="list-style-type: none"> <li>• <b>Life-threatening generalized anaphylactic reaction:</b> 0.02% patients (1/4612) <ul style="list-style-type: none"> <li>• Reaction occurred within minutes of completing the procedure; patient recovered fully</li> </ul> </li> <li>• <b>Grand mal seizure:</b> 0.02% patients (1/4612) <ul style="list-style-type: none"> <li>• Occurred within 10 seconds of therapeutic injection of medication; lasted 3-4 minutes; patient recovered completely within 30 minutes without any medications beyond nasal oxygen and IV saline</li> </ul> </li> <li>• <b>Nerve root injury/infarct:</b> 0% patients (0/4612)</li> <li>• <b>Spinal cord injury/infarct:</b> 0% patients (0/4612)</li> <li>• <b>Brain stem injury/infarct:</b> 0% patients (0/4612)</li> <li>• <b>Cerebellar/cerebral injury/infarct:</b> 0% patients (0/4612)</li> <li>• <b>Infection:</b> 0% patients (0/4612)</li> </ul>
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<p><b>Waldman (1989)</b></p>	<p>Case series (prospective)</p> <p>N = 215 (790 injections)</p> <p>Diagnosis varied (65.4% cervical radiculopathy; 19.6% cervicalgia/cervical strain; 4.6% muscle contraction headache; 3.9% post herpetic neuralgia; 3.9% pain of malignant origin; 3.2% reflex sympathetic dystrophy)</p> <p>Duration of symptoms: NR</p> <p>Mean age: 43 years (range, 16-92 years)</p> <p>53% female</p>	<p>Immediate post-procedural, 3 &amp; 6 weeks follow-up (89.3% (192/215))</p>	<p>Cervical epidural steroid nerve block (NO fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> methylprednisolone (80 mg for first injection; 40 mg for subsequent injections; 20 mg after first injection if multiple injections performed simultaneously)</p> <p><u>Repeat injections:</u> Mean 3.7 injections per patient (range, 1-9) (performed on alternate days except in patients with acute herpes zoster or severe reflex sympathetic dystrophy, who received injections every day)</p> <p><u>Cointerventions:</u> NR</p>	<p><b><u>Minor complications:</u></b></p> <ul style="list-style-type: none"> <li>• <b>Any complication:</b> NR</li> <li>• <b>Vasovagal reaction:</b> 1.6% patients (3/192) <ul style="list-style-type: none"> <li>• Occurred during first block; two patients required intravenous fluids and ephedrine; no long-term sequelae, patients resumed blocks with intravenous fluids and ephedrine (25 mg) given prior to procedure</li> </ul> </li> <li>• <b>Dural puncture &amp; associated headache:</b> 1.0% patients (2/192) <ul style="list-style-type: none"> <li>• Patients treated with cervical epidural (autologous) blood and bedrest; symptoms resolved within 24-72 hours</li> </ul> </li> <li>• <b>Superficial infection/abscess at injection site:</b> 0.5% patients (1/192) <ul style="list-style-type: none"> <li>• Required incision/drainage and treated with antibiotics; patient recovered without sequelae</li> </ul> </li> </ul>
<p><b>Lumbar + cervical (mixed)</b></p>				

<p><b>Huston (2005)</b></p>	<p>Prospective cohort study</p> <p>N = 211 (306 injections)</p> <p>Cervical OR lumbar pain; specific diagnosis NR (likely included radicular pain)</p> <p>Duration of pain (mean): NR</p> <p>Mean age: 48.5 years (range, 15-90 years)</p> <p>58.7% female</p>	<p>Procedural, post-procedure, 1 week (100% f/u); 3 weeks (99% f/u; 209/211)</p> <p>Follow-up data for control group collected at 1 week only</p>	<p>Selective nerve root injection (fluoroscopy guidance) (steroid + local anesthetic) (n = 151 (lumbar: 114/151; cervical, 37/151)) <u>vs</u> no injection (control) (n = 60)</p> <p><u>Steroids used:</u> Betamethasone (mg NR)</p> <p><u>Repeat injections:</u> 1-3 injections (mean: 2.0 injections per patient in the tx group)</p> <p><u>Cointerventions:</u> Analgesics, anti-inflammatory medications and physical therapy referral</p>	<p><b>Selective nerve root injection (n = 151) vs no tx control (n = 60)‡:</b> (all data reported for patients at 1 week unless otherwise noted)</p> <ul style="list-style-type: none"> <li>• <b>Overall rate of any complaints:</b> 80% patients (121/151) versus 97% patients (58/60) (<math>P = .003</math>)</li> <li>• <b>Vasovagal:</b> 0% versus 0%</li> <li>• <b>Dural puncture:</b> <ul style="list-style-type: none"> <li>• <b>Procedural:</b> 0.7% (1/151) (cervical injection) versus n/a</li> <li>• <b>1 week:</b> 0% versus n/a</li> </ul> </li> <li>• <b>Increased spine pain:</b> 37% (56/151) versus 33% (20/60) (ns)</li> <li>• <b>Increased radicular pain:</b> 37% (56/151) versus 36% (21/60) (ns)</li> <li>• <b>Increased pain at injection site:</b> 30% (46/151) versus 8% (5/60) (<math>P = .001</math>)</li> <li>• <b>Increased pain:</b> 15% (22/151) versus 22% (13/60) (ns)</li> <li>• <b>Lightheadedness:</b> 19% (29/151) versus 27% (16/60) (ns)</li> <li>• <b>Nausea:</b> 17% (26/151) versus 10% (6/60) (ns)</li> <li>• <b>Numbness (distribution of nerve block):</b> 6% (9/151) versus n/a</li> <li>• <b>Numbness (lower extremity):</b> 11% (17/151) versus 32% (19/60) (ns)</li> <li>• <b>Numbness (upper extremity):</b> 2% (3/151) versus 8% (19/60) (<math>P = .024</math>)</li> <li>• <b>Headache (nonspecific, not spinal):</b> 8% (12/151) versus 2% (1/60) (ns)</li> <li>• <b>Headache (increased with standing):</b> 5% (8/151) versus 2% (1/60) (<math>P = \text{NR}</math>)</li> <li>• <b>Headache (<u>not</u> increased with standing):</b> 18% (27/151) versus 12% (7/60) (ns)</li> <li>• <b>Fluid retention:</b> 8% (12/151) versus 23% (14/60) (<math>P = .002</math>)</li> <li>• <b>Agitation:</b> 17% (25/151) versus 53% (32/60) (<math>P = .001</math>)</li> <li>• <b>Insomnia (pain related):</b> 11% (17/151) versus 38% (23/60) (<math>P = .001</math>)</li> <li>• <b>Insomnia (<u>not</u> pain related):</b> 9% (14/151) versus 40% (24/60) (<math>P = \text{NR}</math>)</li> <li>• <b>Weight gain:</b> 7% (11/151) versus 0% (<math>P = \text{NR}</math>)</li> <li>• <b>Fatigue/malaise:</b> 19% (28/151) versus 43% (26/60) (<math>P = .001</math>)</li> <li>• <b>Esophagitis/gastritis- heartburn:</b> 24% (36/151) versus 28% (17/60) (ns)</li> <li>• <b>Facial or chest flushing:</b> 19% (29/151) versus 13% (8/60) (ns)</li> <li>• <b>Hearing loss:</b> 1% (2/151) versus 7% (4/60) (<math>P = \text{NR}</math>)</li> </ul>
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<b>Johnson (1999)</b>	<p>Case series (retrospective)</p> <p>N = 5334 patients (5334 injections)</p> <p>Back or neck pain with or without radiculopathy</p> <p>Duration of pain (mean): NR</p> <p>Mean age: NR</p> <p>Sex: NR</p>	<p>Immediate postprocedural data (100% f/u); patients instructed to call proceduralist if any side effects or complications occur within 2 weeks of injection</p>	<p>Epidural injection (approach varied) (~87.1% lumbar, ~12.2% cervical, ~0.7% thoracic) (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> NR</p> <p><u>Repeat injections:</u> NR</p> <p><u>Cointerventions:</u> NR</p>	<ul style="list-style-type: none"> <li>• <b>Overall complication rate:</b> 0.075% patients/injections (4/5334)</li> <li>• <b>“Significant” transient hypotensive episode:</b> 0.019% patients/injections (1/5334)</li> <li>• <b>Epidural hematoma:</b> 0.019% patients/injections (1/5334) (resolved within 18 hours without any intervention; no spinal cord or neural compression)</li> <li>• <b>Vasovagal response (severe):</b> 0.019% patients/injections (1/5334) (resolved without treatment)</li> <li>• <b>Tachycardia + hypertension:</b> 0.019% patients/injections (1/5334) (resolved after 3 days in hospital)</li> <li>• <b>Infection:</b> 0% patients/injections</li> <li>• <b>Delayed complications/infections (2 years f/u of 150 consecutive pts):</b> 0% patients (0/150) (details NR)</li> </ul>
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<p><b>Stretanski (2005)</b></p>	<p>Case series (retrospective)</p> <p>N = 450 (1295 injections)</p> <p>Diagnosis: NR</p> <p>Duration of pain (mean): NR</p> <p>Mean age: 57 years (range, 19-96 years)</p> <p>55.3% female</p>	<p>Procedural data (100% f/u)</p>	<p>Spinal injection (approach varied)</p> <p><u>Lumbar</u>: 36.1% injections interlaminar (translaminar), 13.7% injections transforaminal, 11.6% injections facet, 13.7% injections sacroiliac joint</p> <p><u>Cervical</u>: 7.7% nterlaminar (translaminar), 8.3% facet</p> <p><u>Other</u>: 1.0% lumbar sympathetic block, 4.3% intercostal nerve block, 3.5% caudal with catheter</p> <p>(fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used</u>: NR</p> <p><u>Repeat injections</u>: NR</p> <p><u>Cointerventions</u>: NR</p>	<ul style="list-style-type: none"> <li>• <b>Subdural/subarachnoid injections</b>: 0% patients (0/450), 0% injections (0/1295)</li> <li>• <b>Chest pain</b>: 0.2% patients (1/450) <ul style="list-style-type: none"> <li>• Cervical injection, patient had history of chronic airway disease, patient transferred to emergency room (no other details reported)</li> </ul> </li> <li>• <b>Nausea</b>: 0.2% patients (1/450) <ul style="list-style-type: none"> <li>• Required intramuscular promethazine</li> </ul> </li> </ul>
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CMM: conservative medical management

f/u: follow-up

HNP: herniated nucleus pulposus

LBP: lower back pain

LSS: lumbar spinal stenosis

n/a: not applicable

NR: not reported

ns: not statistically significant

SD: standard deviation

\* f/u data reflects only patients with complete follow-up

† Bowin 2001: authors included the 11 patients (11 injections) with incomplete follow-up in their results (report results for 139 pts (257 injections) even though they had complete follow-up of 128 patients (246 injections)).

‡ Huston 2005: the percentages reported in the study did not correspond to whole patient numbers. We calculated patient numbers using the percentages reported in the study; when patient numbers were obtained, we rounded to the nearest whole patient number and then recalculated the percent. In some cases, this resulted in slight changes in the percentages compared with what the study reported.

§ Huston 2005: increased pain at injection site reported for control group even though no injection was received.

**Appendix T. Data from non-randomized studies designed to assess the incidence of vascular puncture.**

Author (Year)	Study type  Sample size (N)  Diagnosis Duration of symptoms Mean age (range) Sex	Duration of follow-up (% complete follow-up rate)	Interventions	Complications
<b>Lumbar</b>				
<b>Furman (2000)</b>	Case series (prospective)  N = 670 (761 injections)  Lumbar disc pathology or spinal stenosis  Duration of pain (mean): NR  Mean age: 53 years (range, 14-87 years)  50.9% female	Procedural data only (100% f/u)	Transforaminal lumbosacral epidural injection (fluoroscopic guidance) (steroid + local anesthetic)  <u>Steroids used:</u> NR  <u>Repeat injections:</u> none  <u>Cointerventions:</u> NR	<ul style="list-style-type: none"> <li>• <b>Intravascular injection:</b> 11.2% injections (85/761) (prediction of positive intravascular injection by flash or aspiration of blood was accurate in 38/85 cases; prediction of negative intravascular injection was accurate in 662/676 injections).</li> </ul>

<p><b>Goodman (2005)</b></p>	<p>Case series (prospective)</p> <p>N = 160 (280 injections)</p> <p>Duration of pain (mean): NR</p> <p>Mean age: NR</p> <p>Sex: NR</p>	<p>Procedural data only (100% f/u)</p>	<p>Intradiscal injection (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Triamcinolone acetonide (<math>\leq</math> 120 mg)</p> <p><u>Repeat injections:</u> none</p> <p><u>Cointerventions:</u> NR</p>	<ul style="list-style-type: none"> <li>• <b>Intravascular injection (uptake):</b> 14.3% injections (40/280)</li> <li>• <b>Flash/aspiration of blood:</b> performed but results NR</li> </ul>
<p><b>Manchikanti (2004)</b> <b>Evaluation of fluoroscopically guided...</b></p>	<p>Case series (prospective)</p> <p>N = 100 (256 injections)</p> <p>Low back pain due to disc degeneration, facet arthropathy, spinal stenosis, disc bulging, disc protrusion, disc herniation, epidural fibrosis, or no diagnosed abnormalities</p> <p>Duration of pain (mean): NR</p> <p>Mean age: NR</p> <p>62% female</p>	<p>Procedural data only (100% f/u)</p>	<p>Caudal epidural injection (needle placed without fluoroscopic guidance; needle position checked with fluoroscopy/contrast injection) (details on medication NR)</p> <p><u>Steroids used:</u> NR</p> <p><u>Repeat injections:</u> none</p> <p><u>Cointerventions:</u> NR</p>	<ul style="list-style-type: none"> <li>• <b>Vascular puncture (needle placement):</b> 14% patients (14/100), % injections NR</li> <li>• Needle repositioned prior to injecting medication, so intravascular uptake was avoided</li> <li>• prediction of positive intravascular injection by flash or aspiration of blood was accurate in 7/14 cases; prediction of negative intravascular injection was NR</li> </ul>

<p><b>Manchikanti (2004)</b> <b>Evaluation of lumbar...</b></p>	<p>Case series (prospective)</p> <p>N = 100 (256 injections)</p> <p>Low back pain due to disc degeneration, facet arthropathy, spinal stenosis, disc bulging, disc protrusion, disc herniation, epidural fibrosis, or no diagnosed abnormalities</p> <p>Duration of pain (mean): NR</p> <p>Mean age: NR</p> <p>60% female</p>	<p>Procedural, post-procedure, 24-72 hours (100% f/u)</p>	<p>Transforaminal epidural injection (fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used:</u> Betamethasone acetate/Betamethasone sodium phosphate (3-6 mg)</p> <p><u>Repeat injections:</u> none</p> <p><u>Cointerventions:</u> NR</p>	<ul style="list-style-type: none"> <li>• <b>Vascular puncture (needle placement):</b> 22% injections (57/256) <ul style="list-style-type: none"> <li>• Needle repositioned prior to injecting steroid/anesthetic, so intravascular uptake was avoided</li> <li>• prediction of positive intravascular injection by flash or aspiration of blood was accurate in 45/57 cases; prediction of negative intravascular injection was NR</li> </ul> </li> </ul>
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<b>Sullivan (2000)</b>	<p>Case series (prospective)</p> <p>N = NR (1219 injections)</p> <p>Diagnosis NR</p> <p>Mean age: NR</p> <p>55.3% injections were performed on women</p>	<p>Procedural data only (100% f/u)</p>	<p>Spinal injections (approach varied) (55.2% injections transforaminal, 17.0% injections interlaminar (translaminar), 10.6% injections caudal, 10.9% injections facet joint, 6.3% injections sacroiliac joint) (fluoroscopic guidance) (medication- details NR)</p> <p><u>Steroids used:</u> NR</p> <p><u>Repeat injections:</u> NR</p> <p><u>Cointerventions:</u> NR</p>	<ul style="list-style-type: none"> <li>• <b>Vascular puncture (needle placement):</b> 8.5% injections (104/1219) <ul style="list-style-type: none"> <li>• Vascular puncture was detected by vascular patterning during real-time injection of contrast agent</li> <li>• Needle repositioned prior to injecting steroid/anesthetic, so intravascular uptake was avoided</li> </ul> </li> </ul>
<b>Cervical</b>				
<b>Furman (2003)</b>	<p>Case series (prospective)</p> <p>N = 337 (504 injections)</p> <p>Cervical disc pathology</p> <p>Duration of symptoms: NR</p> <p>Mean age: 49 years (range, 24-88 years)</p> <p>56.3% female</p>	<p>Procedural data only (100% f/u)</p>	<p>Transforaminal epidural injection (fluoroscopic guidance) (steroid)</p> <p><u>Steroids used:</u> NR</p> <p><u>Repeat injections:</u> Details NR</p> <p><u>Cointerventions:</u> NR</p>	<ul style="list-style-type: none"> <li>• <b>Vascular puncture (needle placement):</b> 19.4% injections (98/504) <ul style="list-style-type: none"> <li>• Study of incidence of vascular puncture was detected by vascular patterning during real-time injection of contrast agent</li> <li>• No other safety outcomes reported</li> </ul> </li> <li>• <b>Flash or positive aspiration (observed blood in the needle hub):</b> <ul style="list-style-type: none"> <li>• Sensitivity: 45.9% (accurately predicted 45/98 cases of confirmed intravascular injections)</li> <li>• Specificity: 97.0% (accurately predicted 394/406 cases of confirmed nonvascular injections)</li> </ul> </li> </ul>
<b>Lumbar vs cervical</b>				

<p><b>Stretanski (2005)</b></p>	<p>Case series (retrospective)</p> <p>N = 450 (1295 injections)</p> <p>Diagnosis: NR</p> <p>Duration of pain (mean): NR</p> <p>Mean age: 57 years (range, 19-96 years)</p> <p>55.3% female</p>	<p>Procedural data (100% f/u)</p>	<p>Spinal injection (approach varied)</p> <p><u>Lumbar</u>: 36.1% injections interlaminar (translaminar), 13.7% injections transforaminal, 11.6% injections facet, 13.7% injections sacroiliac joint</p> <p><u>Cervical</u>: 7.7% interlaminar (translaminar), 8.3% facet</p> <p><u>Other</u>: 1.0% lumbar sympathetic block, 4.3% intercostal nerve block, 3.5% caudal with catheter</p> <p>(fluoroscopic guidance) (steroid + local anesthetic)</p> <p><u>Steroids used</u>: NR</p> <p><u>Repeat injections</u>: NR</p> <p><u>Cointerventions</u>: NR</p>	<ul style="list-style-type: none"> <li>• <b>Vascular puncture (needle placement)</b>: 8.4% injections (109/1295), 17.3% patients (78/450) <ul style="list-style-type: none"> <li>• Vascular puncture was detected by vascular patterning during real-time injection of contrast agent</li> <li>• Needle repositioned prior to injecting steroid/anesthetic, so intravascular uptake was avoided</li> </ul> </li> </ul>
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CMM: conservative medical management

f/u: follow-up

HNP: herniated nucleus pulposus

LBP: lower back pain

LSS: lumbar spinal stenosis

NR: not reported

ns: not statistically significant

SD: standard deviation

### Appendix U. Summary of the incidence of vascular puncture.

Study	Fluoroscopic guidance during needle positioning?	Incidence of intravascular injection (% injections)	Sensitivity of flash/blood aspiration as a predictor (% injections)
<b>LUMBAR</b>			
<b>Any type of lumbar injection</b>	Yes*	10.18%* (359/3526) (5 studies) <sup>63, 70, 122, 195, 196</sup>	44.3% *† (108/244) (3 studies) <sup>63, 122, 196</sup>
<b>Epidural, transforaminal</b>			
Furman (2000) <sup>63</sup>	Yes	11.2% (85/761)	45% (38/85)
Manchikanti (2004) (Evaluation of lumbar...) <sup>122</sup>	Yes	22% (57/256)	79% (45/57)
Sullivan (2000) <sup>196</sup>	Yes	10.8% (72/669)	25% (18/72)
Stretanski (2005) <sup>195</sup>	Yes	12.4% (22/178)	NR
<b>Epidural, caudal</b>			
Manchikanti et al (2004) (Evaluation of fluoroscopically guided...) <sup>123</sup>	No	14% patients (14/100) (% injections NR)	50% patients (7/14)
Sullivan et al (2000) <sup>196</sup>	Yes	10.9% (14/128)	36% (5/14)
Stretanski (2005) <sup>195</sup>	Yes	16% (7/45)	NR
<b>Epidural, interlaminar</b>			
Sullivan et al (2000) <sup>196</sup>	Yes	1.9% (4/206)	50% (2/4)
Stretanski (2005) <sup>195</sup>	Yes	3.8% (18/468)	NR
<b>Facet joint</b>			
Sullivan et al (2000) <sup>196</sup>	Yes	6.1% (8/132)	0% (0/8)
Stretanski (2005) <sup>195</sup>	Yes	8.7% (13/150)	NR
<b>Sacroiliac joint</b>			
Sullivan et al (2000) <sup>196</sup>	Yes	5.3% (4/76)	0% (0/4)
Stretanski (2005) <sup>195</sup>	Yes	8.5% (15/177)	NR
<b>Intradiscal</b>			
Goodman et al (2005) <sup>70</sup>	Yes	14.3% (40/280)	NR
<b>CERVICAL</b>			

<b>Any type of lumbar injection</b>	Yes	15.6% (113/712) (2 studies) <sup>62, 195</sup>	45.9% (45/98) (1 study) <sup>62</sup>
<b>Epidural, transforaminal</b>			
Furman (2003) <sup>62</sup>	Yes	19.4% (98/504)	45.9% (45/98)
<b>Epidural, interlaminar</b>			
Stretanski (2005) <sup>195</sup>	Yes	4.0% (4/100)	NR
<b>Facet joint</b>			
Stretanski (2005) <sup>195</sup>	Yes	10.2% (11/108)	NR

\* does not include Manchikanti et al (2004) (Evaluation of fluoroscopically guided...) (reports % patients only)

† does not include Goodman (2005) (did not report % specificity) or Manchikanti (2004) (Evaluation of fluoroscopically guided...) (reports % patients only)

### Appendix V. Data from studies evaluating the cost-effectiveness of spinal injections.

Study (year) country	Study design	Model details/assumptions	Sensitivity analysis	Relevant results	Author conclusions
Karpainen (2001), Finland	<p>Measurement of costs alongside double-blind randomized controlled trial</p> <p>Intervention: epidural injection methylprednisolone bupivacaine combo (steroid)</p> <p>Comparator: epidural injection of saline</p> <p>Population: 160 people with sciatica of 1-6 months duration and never had surgery</p> <p>Outcomes assessed at 2 weeks, 4 weeks, 6, and 12 months; costs assessed at 4 weeks and 12 months</p>	<p><b>Outcomes:</b> VAS leg and back pain; Oswestry score; Nottingham health profile; mean duration of sick leave; straight leg raising test; lumbar flexion; motor deficit</p> <p><b>Costs:</b> National Insurance Register; study questionnaires; medical records; study hospital charges; home help (spouse, relative, friend) estimated from average wage of home helper. Value of sick leave not assessed.</p>	None	<p><b>Outcomes:</b> By 12 months, no significant outcome differences between intervention and saline groups.</p> <p>At 2 weeks, more improvement in leg pain, straight leg raising, and lumbar flexion, and patient satisfaction in intervention group (<math>p \leq 0.05</math>); at 3 and 6 months saline group showed improved back and leg pain (<math>p &lt; 0.05</math>)</p> <p><b>Costs:</b> No significant differences in total mean cost at 4 weeks (\$858 for steroid group; \$827 for saline group) or 12 months (\$2195 for steroid group; \$2180 for saline group)</p> <p>At 4 weeks: steroid group fewer therapy visits (0.4 vs 1.9, \$12 vs \$59, <math>P = 0.05</math>), lower medication costs (\$4 vs \$11, <math>P = 0.005</math>)</p>	“Methylprednisolone treatment produced savings in costs of therapy visits and medications at 4 weeks, but other uses of resources and their respective costs and mean duration of sick leave were more or less equal in the two groups throughout the followup period.”
Price 2005, UK HTA	Cost utility analysis using data from a pragmatic prospective multicenter double blind RCT (Arden 2005)	<p>Outcomes: Pain relief and physical/psychological function; Oswestry Disability Questionnaire; SF-6D (from SF-36)</p>	Cost per patient estimates recalculated to maximum values across RCT (purchaser costs not varied)	<p>ESI benefit in ODQ and pain relief at 3 weeks (<math>p = 0.017</math>, <math>NNT = 11.4</math>); no benefit of ESI between weeks 6-52.</p> <p>No significant</p>	

	<p>Intervention: Up to 3 epidural steroid injections (ESI)</p> <p>Comparator: saline injection</p> <p>12 month follow up (survey 3 months)</p> <p>Population: 228 people with acute (&lt;4 months) or chronic (4-18 months) unilateral sciatica, age 18-70yrs</p>	<p>Costs (provider perspective): clinician time for assessment, procedure, recovery, drug and equipment use, pathology and radiology use. Costs estimated from NHS Trust.</p> <p>Costs (purchaser perspective): Cost per patient for RCT protocol and for only one injection per results of RCT; total costs including overheads</p>		<p>differences between ESI and placebo for any other outcomes.</p> <p>2.2 days of full health=incremental 1 QALY improvement for ESI</p> <p>Cost per patient for trial protocol: £265 provider perspective; £2102 purchaser perspective</p> <p>ICER from purchaser perspective: £354,171/QALY for trial protocol; £167,145/QALY for one ESI</p> <p>ICER from provider perspective: £44,701/QALY for trial protocol; £25,745 for one ESI</p>	
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## Appendix W. CLINICAL PEER REVIEWERS

Reviewer	Areas of expertise
<p><b>Janna Friedly, M.D.</b>  Assistant Professor  Medical Director- Outpatient Rehabilitation  Medicine Clinics  Departments of Rehabilitation Medicine,  Comparative Effectiveness, Cost and  Outcomes Research Center  University of Washington/ Harborview Medical  Center</p>	<p>Research areas:</p> <ul style="list-style-type: none"> <li>• Health services and outcomes research</li> <li>• Low back pain</li> <li>• Chronic pain</li> <li>• Epidural steroid injections</li> </ul> <p>Clinical expertise:</p> <ul style="list-style-type: none"> <li>• Amputation/limb loss</li> <li>• Trauma rehabilitation</li> <li>• Chronic pain</li> </ul>
<p><b>Laxmaiah Manchikanti, M.D.</b>  Medical Director- Pain Management Center of  Paducah  Associate Clinical Professor  Anesthesiology and Perioperative Medicine  University of Louisville, Kentucky</p>	<ul style="list-style-type: none"> <li>• Interventional pain management</li> <li>• Spinal injections</li> <li>• Spinal disorders</li> <li>• Chronic pain</li> </ul>